The redox couple involving NOx in aerobic Pd-catalyzed oxidation of sp3-C–H bonds: direct evidence for Pd-NO3–/NO2– interactions involved in oxidation and reductive elimination

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ABSTRACT: NaNO3 is used in oxidative Pd-catalyzed processes as a complementary co-catalyst to common oxidants, *e.g.* CuII salts, in C-H bond activation and Wacker oxidation processes. NaNO3 and NaNO2 (with air or O2) assist the sp3-C-H bond acetoxylation of substrates bearing an N-directing group. It has been proposed previously that a redox couple is operative. The role played by ‘NOx’ anions is examined in this investigation. Evidence for an NOx anion interaction at PdII is presented. Palladacyclic complexes containing NOx anions are competent catalysts for acetoxylation of 8-methylquinoline, with and without exogenous NaNO3. The oxidation of 8-methylquinoline to the corresponding carboxylic acid has also been noted at PdII. 18O-labeling studies indicate that oxygen derived from nitrate appears in the acetoxylation product, the transfer of which can only occur by interaction of 18O at Pd with a coordinating-acetate ligand. Nitrated organic intermediates are formed under catalytic conditions, which are converted to acetoxylation products, a process which occurs with (50 °C) and without Pd (110 °C). A catalytically competent palladacyclic dimer intermediate has been identified.Head-space analysis measurements show that NO and NO2 gases are formed within minutes on heating catalytic mixtures to 110 °C from room temperature. Measurements by *in situ* infrared spectroscopy show that N2O is formed in sp3-C-H acetoxylation reactions at 80 °C. Studies confirm that cyclopalladated-NO2 complexes are rapidly oxidized to the corresponding NO3 adducts on exposure to NO2(g). The investigation shows that NOx anions act as participating ligands at PdII in aerobic sp3-C-H bond acetoxylation processes, and are involved in redox processes.

Introduction

The catalytic and selective C–H bond functionalization of organic substrates is of fundamental importance in synthetic chemistry.[[1]](#endnote-1) Significant effort has been directed toward solving the issue of challenging C–H bond functionalization reactions in a variety of substrates. Whilst much has been accomplished in the field of selective C(sp2)–H functionalizations, reactions of less-activated C(sp3)–H bonds, *e.g.* as found in secondary and tertiary alkyls, allylic and benzylic systems, has proven more challenging. In driving the development of challenging C(sp3)–H bond functionalization processes, mechanistic studies (both experimental and computational) are essential – the key role played by a particular metal, ligand (neutral or anionic), additive or specific substrate class, under an eclectic array of reaction conditions, cannot be understated. These points are evidenced from a series of recent studies exploiting the redox activity of nitrate (NO3–) and/or nitrite (NO2–) anions, *vide infra*. In C-H bond functionalization chemistry, the role of such anions at Pd is poorly defined, requiring mechanistic examination, particularly if the catalytic behavior of reaction processes utilizing these anions is to be fully realized. Of particular note is the work of Stahl and co-workers who reported selective benzene acetoxylation using NOx-based redox mediators at Pd.[[2]](#endnote-2)

Sanford and co-workers[[3]](#endnote-3) reported a remarkable methodology for the acetoxylation of unactivated C(sp3)–H bonds, *i.e.* inoxime ether and pyridine-type derivatives, with the nitrogen atom playing the role of directing group to Pd. The reactions utilized Pd(OAc)2 as a catalyst and dioxygen as the terminal oxidant in acetic acid (AcOH)/acetic anhydride (Ac2O) (Fig. 1). Vedernikov and co-workers reported a similar oxidative catalyst process using PdII-pyridinecarboxylic acid systems.[[4]](#endnote-4)



**Fig. 1** Proposed mechanism for C(sp3)–H bond-functionalization3 using a NOx redox-couple at Pd.

Addition of NaNO3 – proposed to be a redox co-catalyst3 – was important for effective catalysis (NO was detected, formed by decomposition of NaNO3 and it is of note that NaNO2 can play a similar activating role). Using 18O-labeled dioxygen, it was deduced that oxygen-incorporation into the acetoxylated product derives from acetic acid (solvent) and not O2. A key question that we asked was are NO3– and/or NO2– critical ligands (pseudohalides) at Pd within the catalytic cycle? And, if Pd-NO3/Pd-NO2 species are present, then C-O bond-formation ought to be favored over C-N bond formation as acetoxylated products are the only ones observed, despite reductive elimination of ‘NO2’ being feasible at Pd.

Examining the role played by NO3– /NO2– anions is arguably essential for the development of other redox-coupled Pd catalysis, particularly as nitrite (AgNO2) has been shown to be directly involved in a recently-developed catalyst-controlled Wacker Oxidation.[[5]](#endnote-5) Grubbs and Stoltz further reported Pd-catalyzed aerobic intramolecular aminoacetoxylation of alkenes enabled by Cu(NO3)2, the latter acting as an electron transfer mediator.[[6]](#endnote-6) Also, Xu and co-workers demonstrated that MNO3 (M = K or Ag) can act as a co-catalyst in C-H bond fluorination chemistry.[[7]](#endnote-7) Xu proposed the involvement of PdII/PdIV species based on ESI-MS analysis of the catalytic reaction under working conditions. Moreover, they suggested [Pd(NO3)]+ as the active catalyst species, although direct evidence for its existence was not presented. These recent findings are underpinned by a series of long-standing studies on other catalytic processes involving nitrate/nitrite anions at PdII. For example, formation of ethylene glycol monoacetate from ethylene in acetic acid solution containing LiNO3 and Pd(OAc)2 is accompanied by oxygen atom transfer from the oxidant to the carbonyl group of the product (confirmed by 17O-labeling).[[8]](#endnote-8) Henry reported that NaNO3 and NaNO2 can be used as oxidants in the C(sp2)–H oxidation of various aromatics, where the nitrate/nitrite can play a similar role to Cu.[[9]](#endnote-9) In the 1980s several groups explored the catalytic properties of [Pd(Cl)(NO2)(CH3CN)] in the oxidation of olefins to either epoxides and ketones, as well as glycol mono acetate.[[10]](#endnote-10),[[11]](#endnote-11),[[12]](#endnote-12),[[13]](#endnote-13),[[14]](#endnote-14) Bäckvall and Heumann proposed that the nitrite ligand can be an active ligand at PdII, where the oxygen from ‘PdNO2’ is transferred to the acetoxylated organic product.[[15]](#endnote-15)

The dynamic behavior of nitrite at PdII has been of particular interest to our group[[16]](#endnote-16) and Raithby,[[17]](#endnote-17) *i.e.* ‘Pd-NO2’ and ‘Pd-ONO’ linkage isomerization in various palladium complexes. Indeed, in expanding the scope of our work to understand the intimate role played by nitrite and nitrate at PdII and higher oxidation state Pd species, in addition to the role played by such anions in other catalytic Pd chemistry, we were attracted by the underlying role played by NOx anions in Sanford’s C(sp3)–H bond acetoxylation mediated by PdII/NaNO3,3 in addition to the broader context of the work reported by Grubbs *et al*.5 Herein, we describe our mechanistic findings on the role played by NaNO3­ and ‘Pd-NO2’/’Pd-NO3’ species in the acetoxylation of Csp3-H bonds.

# RESULTS

We selected to direct our mechanistic studies to 8-methylquinoline (**1**). Under the conditions described by Sanford and co-workers {5 mol% Pd(OAc)2, 1 eq. NaNO3, AcOH/Ac2O, air, 110 °C, 18 h} the acetoxylated product (**2**) was formed in 80% yield (Scheme 1).3 The Pd(OAc)2 used throughout this study is Pd3(OAc)6 (verified by IR and NMR; stated as >99% purity by the supplier).[[18]](#endnote-18) In our hands we recorded >99% conversion to **2** by both GC and 1H NMR spectroscopic analysis of the crude reaction, validating it as a starting point for further study.

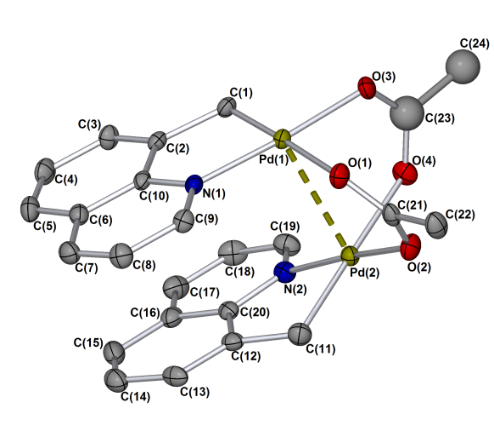
The overwhelming evidence from the field is that the first committed step in the catalytic cycle involves C–Pd bond-formation by C–H bond functionalization (cyclopalladation),[[19]](#endnote-19) likely by a Concerted-Metallation-Deprotonation (CMD) reaction.[[20]](#endnote-20) Stoichiometric reaction of Pd(OAc)2 with **1** (1:1) in AcOH at reflux for 1.5 h gave the novel dinuclear PdII complex (**3**) in 85% yield (Scheme 1).



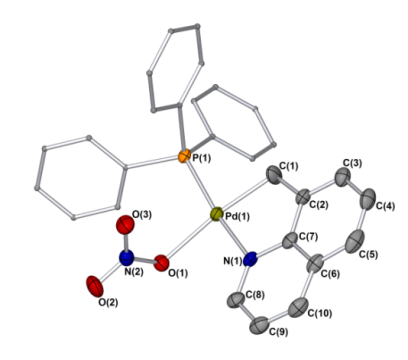
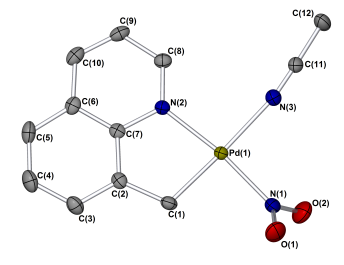
Scheme 1 Synthesis of ‘Pd-NO3’/’Pd-NO2’ complexes.

A single crystal of **3** was grown from CH2Cl2/pentane, and found suitable for X-ray diffraction study, confirming the structure of the cyclopalladated system as a mixture of *syn*/*anti* isomers (Fig. 2), which is consistent with the other characterization data. A prominent feature of the X-ray structure is the slipped π-stacking between quinolinyl groups, which occurs in both *syn*/*anti* isomers. A palladaphilic interaction {dashed line between Pd(1) and Pd(2)} is indicated as the bond distance is within the sum of the Van der Waals radii for the two Pd centers. The introduction of both NO3–/NO2– anions to the PdII centers could be achieved starting from the Cl-bridged dinuclear PdII complex **4** (synthesized in 80% yield by treatment of **3** with LiCl). The mono-nuclear PdII complex **5** was formed quantitatively on treatment of **4** with a slight excess of PPh3. Pd-NO3 (**6a**)and Pd-NO2 (**6b**) mononuclear complexes could be synthesized from **5** by treatment with AgNO3 and AgNO2 respectively.

Complex **6a** was crystallized from CH2Cl2/cyclohexene and its structure was confirmed by single crystal X-ray diffraction (Fig. 3). The NO3 ligand is found *trans* to the sp3-carbon center and *cis* to phosphorus and nitrogen (quinolinyl). The Pd-ONO2 bond distance of Å = 2.125(13) is similar to related complexes.[[21]](#endnote-21) Also, the CH3CN adducts **7a** and **7b** could be synthesized quantitatively from **4**, which were fully characterized. The X-ray structure of **7b** is shown in Fig. 3, which shows that the NO2 ligand is *trans* to nitrogen (quinolinyl). The Pd-NO2 bond distance, Å = 2.006(2), is similar to related Pd complexes reported by our group13a and others.[[22]](#endnote-22)



**Fig. 2** X-ray structure of **3**. Note that the structure is disordered over two positions (only the *anti*-isomer shown here); the C(23) and C(24) atoms are not resolved enough to be displayed as thermal ellipsoids. Selected bond distances (Å) and angles (°): Pd1∙∙∙Pd2 = 2.8408(4), O1-Pd1 = 2.176(3), O2-Pd2 = 2.042(3), O3-Pd1 = 2.058(3), O4-Pd2 = 2.172(4), N1-Pd1 = 2.010(2), N2-Pd2 = 2.005(3), C1-Pd1 = 1.996(3), C11-Pd2 = 2.003(3); C1-Pd1-N1 = 83.96(11), C11-Pd2-N2 = 83.68(12), N2-Pd2-O2 = 173.56(11), N1-Pd1-O3 = 174.82(11).

**Fig. 3** X-ray structures of **6a** (left) and **7b** (right). Selected bond distances (Å) and angles (°) for **6a**: C1-Pd1 = 1.9900(18), N1-Pd1 = 2.0818(14), O1-Pd1 = 2.1250(13), N2-O1 = 1.289(2), N2-O2 = 1.240(2), N2-O3 = 1.232(2), P1-Pd1 = 2.2725(4); C1-Pd1-N1 = 81.61(6), C1-Pd1-O1 = 171.11(6), N1-Pd1-P1 = 175.42(4), O1-Pd1-P1 = 92.66(4). Selected bond distances (Å) and angles (°) for **7b**: C1-Pd1 = 2.009(2), N1-O1 = 1.237(3), N1-O2 = 1.237(3), N1-Pd1 = 2.006(2), N2-Pd1 = 2.0355(19), N3-Pd1 = 2.1185(19); C1-Pd1-N2 = 83.67(8), C1-Pd1-N3 = 177.09(8), N1-Pd1-N2 = 172.26(7).

It did not prove possible to obtain single crystals of either **7a** or **6b** for X-ray crystallography studies. DFT calculations therefore allowed us to assess the single point energies of the possible isomeric structures (see Supporting Information for details). The *trans*-configuration is preferred in complex **7a** (G*cis-trans* = +13 kJ mol-1). For complex **7b**, *cis-* and *trans*-isomeric forms can possess either *N*-bound or *O*-bound nitrite ligands, giving four isomeric possibilities. Both *cis-* and *trans-*isomers containing an *O*-bound nitrite ligand are found to be *ca.* 21-29 kJ mol-1 higher in energy than those containing *N*-bound nitrite ligands. In the latter case however, the *cis*-[Pd(NO2)(C^N)CH3CN] complex is found to be of lower energy than *trans*-[Pd(NO2)(C^N)CH3CN] by 9 kJ mol-1. Reductive elimination of the nitrated ligand backbone, which requires a *cis*-configuration, is feasible from this *cis*-Pd complex *vide infra*.

Taken together, the X-ray structures of **6a** and **7b** and the spectroscopic data for **6b** and **7a** indicate that nitrite and nitrate ligands can coordinate to a PdII center containing a cyclopalladated 8-methylenyl-quinoline.

**Aerobic oxidation of 8-methylquinoline (1).** The reference complexes gathered in Scheme 1, along with the benchmark catalyst Pd(OAc)2, were evaluated in the aerobic oxidation of **1** to give **2** (Fig. 4). For Pd(OAc)2 there was >99% conversion using 1 eq. of NaNO3. The % conversion dropped to 45% using 0.1 eq. of NaNO3 and negligible conversion was noted in its absence. The dinuclear PdII complex (**3**) is a catalytically competent species, showing a relatively similar profile to Pd(OAc)2. The PPh3-containing complexes **6a** and **6b** are also viable catalysts, with **6b** being more active under the conditions using 1 eq. of NaNO3. Complexes **3**, **6a** and **6b** are not catalytically competent in the absence of NaNO3. The stand-out result from Fig. 4 is the catalyst efficacy of complex **7a**, which gave product **2** with 24% conversion (*ca.* 5 catalytic turnovers) in the absence of NaNO3 and air as the oxidant. The reaction mediated by **7a** was found more effective under 1 atm. of O2, leading to a 36% conversion to **2** (*ca.* 7 catalytic turnovers). The effect of nitrate at PdII is therefore confirmed by this observation. The reason for the lack of activity of **6a** and **6b** is likely due to the phosphine ligand altering the kinetics of the catalytic process, particularly comparing directly **6a** with **7a** (CH3CN being more labile than PPh3).[[23]](#endnote-23) Complex **7b**, containing the nitrite ligand, was inactive without NaNO3.

A further series of reactions (**1**→**2**) were conducted using **7a** as the catalyst with varying equivalents of NaNO3 under an atmosphere of either air or O2 (Fig. 5; for completeness, selected data from Fig. 4 is included to reveal the essential trends). From these data complex **7a** is found to be a viable catalyst, especially when using lower equivalents of NaNO3.

Finally, the effect of the nitrate equivalents on **7a** revealed that the relative drop in % conversion to **2** was more pronounced under air, whereas an absolute drop is evidenced under O2 (1 atm.). Good % conversions were observed between 0.05 and 0.1 eq. NaNO3.



**Fig. 4** Catalytic activity of Pd complexes **3**, **6a**, **6b**, **7a** and **7b** compared against Pd(OAc)2 (5 mol%) with varying equivalents of NaNO3, in the aerobic oxidation of **1** to give **2** (conditions: AcOH/Ac2O, 110 °C, air, as for Scheme 1; conversion percentage relates to **2**).



**Fig. 5** Catalytic activity of Pd complex **7a**, with varying equivalents of NaNO3 in the presence of either air or O2, in the aerobic oxidation of **1** to give **2** (other conditions as for Fig. 4).

It is worthy of note that ceric ammonium nitrate (CAN; [(NH4)2Ce(NO3)6]) can be used as a co-catalyst in place of NaNO3. CAN is known to generate NO3● radicals, which are powerful one-electron oxidants.[[24]](#endnote-24) The reaction of **1**→**2** mediated by Pd(OAc)2 (5 mol%), AcOH/Ac2O (7:1), 110 ºC, 24 h and air, in the presence of 0.25 eq. of CAN, gave **2** in 95% yield.

NaN18O3 labeling experiments

The reaction of **1**→**2** mediated by Pd(OAc)2 (5 mol%) was conducted using 1 eq. of NaN18O3 (77.9% 18O-enriched) in AcOH/Ac2O at 110 °C for 24 h under either N2, air or O2. Reactions were essentially quantitative (by GC analysis). For the reaction under N2 (rigorous exclusion of air and degassing using Schlenk technique) the presence of 1 eq. of NaN18O3 efficiently promotes the oxidative process, with 16% 18O incorporation (determined by MS) observed in product **2**. A similar outcome was recorded for the reaction conducted under air (15.6% 18O incorporation; note with a vast excess of AcOH/Ac2O present, if free 18O exchange occurred in solution then the % incorporation would be negligible). In the case of the reaction under an O2 atmosphere negligible 18O incorporation into **2** was recorded. The results suggest that there is an exchange process occurring, *i.e.* the 18O label is washed out of NaN18O3 in the reaction conducted under O2 (*i.e.* into AcOH/Ac2O)­.[[25]](#endnote-25) Under N2 or air the exchange process is diminished leading to some 18O localization into acetoxylation product **2**. The outcome confirms that 18O is transferred from NO3– to Pd to product **2**, confirming its role as an active spectator ligand (note: we have not been able to determine whether the remaining 18O has been transferred to AcOH/Ac2O under the catalytic conditions). One potential pathway showing intramolecular 18O-transfer is given in Scheme 2 – the formation of Pd-O or Pd-OH species may explain the washing out of the 18O label from NaN18O3 in the presence of pure O2. In Sanford’s study,3 18O derived from 18O2 (with unlabeled NaNO3) was transferred into a different acetoxylation product to a small extent (5% 18O incorporation). Taken together with our results this confirms that O2, AcOH/Ac2O and NaNO3 are intimately connected through exchange processes.

**On the involvement of higher oxidation state Pd species.** Higher oxidation state Pd intermediates have been isolated and characterized in related aerobic acetoxylation processes.[[26]](#endnote-26) The incentive for this part of the investigation was to assess whether PdIII or PdIV species could be detected in reactions involving a redox couple and nitrate. As PhI(OAc)2 is a known powerful oxidant in Pd chemistry, we anticipated that it was useful to assess whether higher oxidation state Pd species formed from it were comparable with the Pd-NOx chemistry.



Scheme 2 Incorporation of 18O into acetoxylation product, using NaN18O3 under different conditions (N2/air/ O2); mechanism shows one pathway for 18O incorporation.

Using standard acetoxylation conditions the nitrate oxidant reacts with the *in situ* generated palladacycle. Having previously confirmed palladacycle **3** as catalytically competent,[[27]](#endnote-27) we envisaged that higher oxidation state Pd species, *i.e.* PdIII dinuclear or PdIV mononuclear complexes as depicted in Scheme 3, could be formed by reaction with typical oxidants.26 The reaction of palladacycle **3** with PhI(OAc)2 in AcOH at -12 °C (note: at a substantially lower reaction temperature than the reported catalyzed process3) was monitored by 1H NMR spectroscopy (700 MHz). The consumption of **3** was noted over *ca.* 1.5-2 h with the appearance of acetoxylation product **2** and PhI, but no other Pd intermediates were recorded (see Supporting Information for NMR spectra).

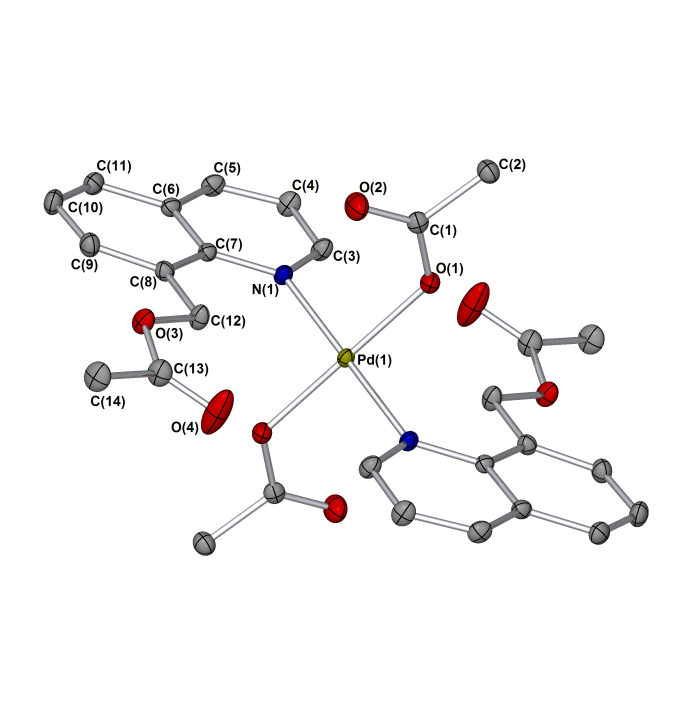


Scheme 3 Reaction of PhI(OAc)2 with palladacycle 3.

A stoichiometric reaction of **3** with NaNO3 was conducted under air at 50 °C in AcOH-*d*4. In comparison with the PhI(OAc)2 reaction conducted at -12 °C, detailed above, a higher temperature was deemed necessary for this stoichiometric reaction to: 1) aid solubility of NaNO3 in AcOH; 2) mirror the working catalytic reaction conditions more closely (without excess **1** to slow down overall catalytic flux27). The time course of the reaction was monitored by 1H NMR spectroscopic analysis (see stacked 1H NMR spectra in Fig. 6). For comparison, reference spectra for substrate **1**, product **2** and complex **3** are included. Within 0.5 h of reaction the proton signals belonging to **3** began to broaden, forming other species which are ill-defined on the NMR timescale. New products were formed after 1.5 h. One of these appears to correspond to **2** (identified by blue arrows) *vide infra*. Another organic product is formed as indicated by a singlet at *ca.* δ 6.20 ppm (highlighted by an orange arrow – see later for confirmation of structure). Other proton signals are observed, the most prominent being that at ~δ 9.4 ppm (highlighted by a green arrow), the complete structure of which could not be discerned. After 2 ha new product (which is **9**) appears possessing 6 correlated proton environments (highlighted by yellow inset boxes).



**Fig. 6** Reaction of **3** with NaNO3 (1 equiv.) in AcOH-*d*4 at 50 °C monitored by 1H NMR spectroscopy (400 MHz). The 1H NMR spectra for reference compounds **1**-**3** are given.



**Fig. 7** The X-ray structure of *trans-*Pd(OAc)2(**2**)­2 (**8**). Selected bond distances (Å) and angles (°) for **8**: N1-Pd1 = 2.0404(14), O1-Pd1 = 2.0064(13); O1-Pd1-N1 = 88.24(5), O1(-X,-Y,1-Z)-Pd1-N1 = 91.76(5), N1-Pd1-N1(-X,-Y,1-Z) = 180.0.

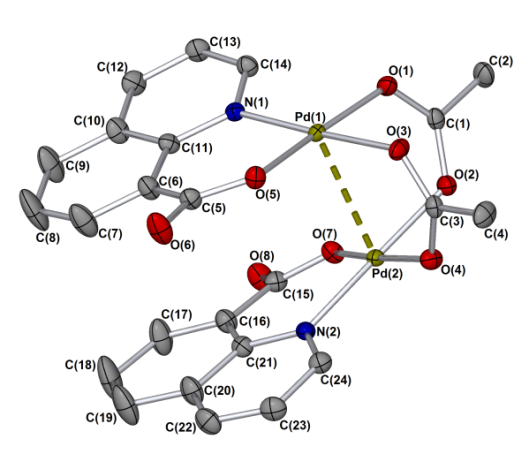
Stopping the reaction at 4 h and crystallization gave two sets of single crystals which were found suitable for X-ray diffraction study. The first crystal recorded was found to be *trans-*Pd(OAc)2(**2**)­2, complex **8** (Fig. 7). This indicates that the species observed by 1H NMR (highlighted by blue arrows) is more likely *trans-*Pd(OAc)2(**2**)­2 (**8**)rather than **2** (confirmed by an authentic 1H NMR spectrum of **8**). The second crystal was determined to be palladacycle **9**, where the ligand backbone had been fully-oxidized to a carboxylate under the conditions of the reaction (Fig. 8; see below for further crystallographic analysis). After 4 h (Fig. 6), only one dominant species remains, which is palladacycle **9**.

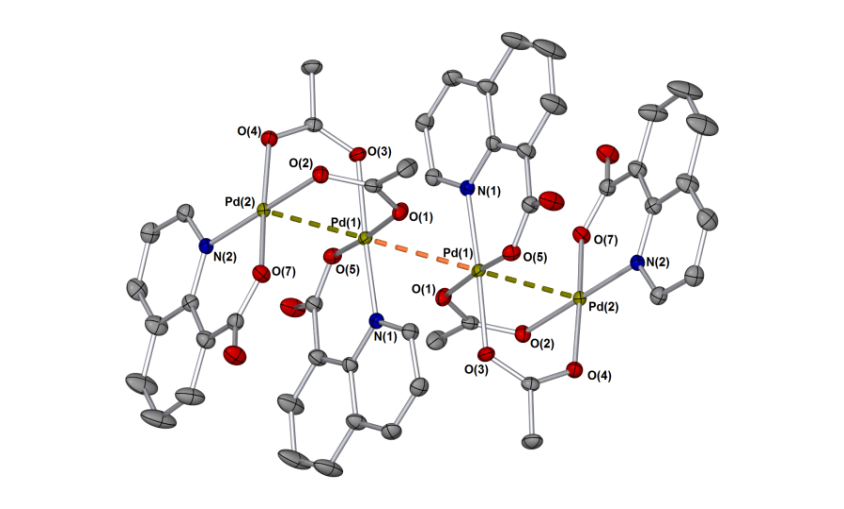
The X-ray structure for palladacycle **9** is found in the P-1 space group (Z = 2). There is evidence of a PdII…PdII interaction – the Pd1-Pd2 distance is 2.7977(2) Å, which is shorter than the Pd1-Pd2 distance in palladacycle **3** {2.8408(4) Å}. In addition, it is pertinent to mention the packing between molecules, which shows that Pd1-Pd1(2-X,1-Y,-Z) is separated by 3.0755(3) Å and Pd2-Pd2(1-X,1-Y,-Z) by 3.0631(3) Å.

A preparative scale reaction of **3** with NaNO3 was conducted, which gave **9** in quantitative yield (Fig. 9). Palladacycle **9** was also accessed by reaction of 8-quinoline carboxylic acid **10** with Pd(OAc)2 (1:1) at 110 °C for 1.5 h, affording **9** in 68% yield.



**Fig. 9** Direct reaction of palladacycle **3** with NaNO3.





**Fig. 8** The X-ray structure of **9** (Top – single molecule; Bottom – showing the packing between molecules and Pd1-Pd1(2-X,1-Y,-Z) interaction). Note that all hydrogens and three molecules of co-crystallized acetic acid are omitted from this drawing. Selected bond distances (Å) and angles (°) for **9**: Pd2∙∙∙Pd1 = 2.7977(2), Pd1-N1 = 1.9931(16), Pd2-N2 = 1.9868(17), Pd1-O3 = 2.0210(13), Pd2-O2 = 2.0189(15); Pd1-O5 = 1.9538(15), Pd2-O7 = 1.9455(13); N1-Pd1-Pd2 = 102.60(4), N2-Pd2-Pd1 = 100.53(5), N1-Pd1-O3 = 177.04(5), N2-Pd2-O2 = 178.17(6).

The minor species present by 1H NMR (see Fig. 6) were of concern to us, particularly as they could not be satisfactorily characterized with the data available. 15N labeling was therefore employed to pursue possible ‘Pd-NOx’ interactions in these minor species. In an otherwise equivalent reaction, palladacycle **3** was reacted with Na15NO3. A 1H{15N} HMQC experiment allowed two clear nitrogen chemical environments (at δ 269 and 340 ppm) to be proton correlated. The major signal observed at δ 6.08 ppm correlates with the 15N signal at δ 340 ppm (Fig. 10). A weaker long range 1H-15N coupling was seen between δ 340 ppm and δ 8.85 ppm (H*Quin*), overlapping with other species). The 15N signal at δ 269 ppm correlates with δ 5.91 and δ 8.29 from the diastereotopic hydrogens of a CH2 (*vide infra*) and 8.63 (H*Quin*). Both of these nitrogen shifts are within the expected range for M-ONO2, M-NO2 and R-NO2 species[[28]](#endnote-28) and the observed signal-to-noise ratio requires that both species are derived from the Na15NO3 and cannot be from the quinoline ligand which is at natural abundance (see Supporting Information).



**Fig. 10** (a) 1H{15N} HMQC NMR spectrum (700 MHz) from the reaction of **3** with Na15NO3 in AcOH-*d*4 after 100 minutes at 80 °C. A 1D 1H spectrum (b) provides a more accurate reflection of the populations of the two 15NOx species; δ(1H) 6.08 ppm (red square, **11**); δ(1H) 5.91 ppm (blue circle, ‘Pd-NOx’ complex) and δ(1H) 5.72 ppm (green triangle, **2**). Note: the signal at 5.72 ppm is shown off-scale.

A repeat experiment to monitor the reaction using natural abundance NaNO3 reveals the 1H signal at 6.08 ppm to be a singlet rather than a doublet (2.1 Hz) and the signal at 5.91 ppm also shows evidence of additional unresolved coupling in the reaction with Na15NO3.

To assist with the characterization of this species, 14/15N NMR spectral data (natural abundance) for a series of compounds (in both CDCl3 and AcOH-*d*4) of interest to this study were collected (Table 1).

Table 1. 15N NMR data for selected compounds in this study (298 K).

|  |  |  |
| --- | --- | --- |
| Compound | δ15N (ppm) | solvent |
| Na15NO3 | 374 | AcOH-*d*4 |
|  | 230 | AcOH-*d*4 |
| 306 | CDCl3 |
|  | 274 | AcOH-*d*4 |
|  | -*a* | AcOH-*d*4 |
| 233 | CDCl3 |
|  | 231 | AcOH-*d*4 |
| 275 | CDCl3 |
|  | 284 (Nquin),  340 (NO2) | AcOH-*d*4 |
|  | 296 (Nquin),  340 (NO2) | AcOH-*d*4 |
| 233 (Nquin),  245 (MeCN)  312 (NO2)b | CDCl3 |
|  | -*c* | AcOH-*d*4 |
| 180 | CDCl3 |
|  | 255 (Nquin)  305 (ONO2)b | CDCl3 |

*a* No 15N signal observed due to dynamic behaviour. *b* Nitrogen shift measured from 1D 14N spectrum. c Insoluble material.

The 15N chemical shift of NO3– isδ 374 ppm in AcOH-*d*4. The quinoline nitrogen (N*quin*) is typically found in the region δ 230-233 ppm (in AcOH-*d*4) in compounds **1**, **3** and **10**, whereas it is δ 274 ppm for compound **2**.The 15N chemical shifts were higher in CDCl3 than AcOH-*d*3 as at the lower pH the quinoline is in equilibrium with the quinolinium ion.[[29]](#endnote-29) Therefore the 15N chemical shift of complex **9** of δ 180 ppm in CDCl3 is likely lower in AcOH-*d*4 – the latter solvent could not be used due to the poor solubility of **9**. The 15N NMR chemical shifts are in keeping with those recently described by Stahl and co-workers.[[30]](#endnote-30) At natural abundance, no 1H-15N correlation could be observed for the NO2 of **7b**, however the 1D 14N (see Supporting Information) in CDCl3 reveals a chemical shift of 312 ppm for the Pd-NO2. In AcOH **7b** is catalytically active and slowly produces **2** (1-2 days). 1H{15N} HMQC spectra (under these conditions revealed a signal δ 340 ppm (15N), which correlates with the methylene protons at δ 6.08 ppm. The observation of the same intermediate, as in the reaction of **3** with Na15NO3, indicates that this species must be formed via a Pd-NO2 species.

The spectrum of **11** showed 1H-15N correlations at δ 6.10, 340 ppm (CH2, NO2) and δ 9.14, 284 ppm (*o*-Hquin, Nquin). Despite the small difference in the 1H shift (ascribed to pH differences of the solution) we assign the (δ 6.08, 340 ppm) signal to compound **11**.

The signal at δ 5.91 ppm (Fig. 10) arises from one of hydrogens of a diastereotopic CH2 group. The signal appears as a doublet with a splitting of 15.5 ­± 0.2 Hz at 16.4 and 9.4 T (700 and 400 MHz 1H, respectively). 1D 1H exchange spectra (tmix = 0.3 s) upon selective irradiation of the signal at 5.91 ppm revealed a signal at δ 8.29 ppm which appears as a doublet with a splitting of 15.5 Hz and is of the same phase as the selectively irradiated signal indicating that it arises due to chemical (EXSY) rather than spin-spin exchange (nOe). A multiplicity-edited 1H{13C} HSQC (see Supporting Information), indicated that both of these hydrogens were attached to “CH2-type” carbons and within the resolution of the experiment, both were attached to the same carbon (78.0 ­± 0.3 ppm). The very high chemical shift of δ 8.29 ppm could be explained by H-bonding with the NOx anion. The only other compound where the methylquinoline CH2 was found to be diastereotopic was the dimeric palladacycle **3** (*anti*-isomer: δ 2.56 and 3.47 ppm, 2*J*=12.9 Hz, *syn*-isomer: δ 3.41 and 3.77 ppm, 2*J*=8.5 Hz). In order to gauge the relative size (solvodynamic radius) of the compound giving rise to the signal at 5.91 ppm a 2D diffusion ordered (DOSY) spectrum was collected. The known species in the reaction mixture (**2**, **11** and AcOD-d4) had diffusion coefficients of 4.21x10-10 m2s-1, 4.92x10-10 m2s-1and, 8.04x10-10 m2s-1 respectively. The signal at 5.91 ppm was found to arise from a complex with a much lower diffusion coefficient, D=2.69x10-10 m2s-1, indicating it is of significantly larger size.

**ESI-MS and LIFDI-MS analysis.** Electrospray ionization mass spectrometry (ESI-MS[[31]](#endnote-31)) is a useful tool for characterizing charged organometallic compounds. Liquid injection field desorption ionization mass spectrometry (LIFDI-MS[[32]](#endnote-32)) can also be used to characterize neutral organometallic species. Both ESI-MS and LIFDI-MS are soft ionization methods, making them suitable for detecting Pd species present under working reaction conditions. Xu and co-workers successfully detected Pd intermediates by ESI-MS in their C-H bond fluorination chemistry.7 The direct ESI-MS analysis of the reaction of palladacycle **3** with NaNO3 in AcOH at 50 °C was conducted. Dissolution of reaction samples in MeOH before electrospray injection facilitated effective ionization. Analysis of a sample after 1 h reaction revealed the presence of a sodiated dinuclear Pd ion **I**, which contains the cyclometallated backbone at Pd, μ-1,3-NO3 and two terminal OMe ligands (Table 2). The observed and calculated isotope patterns for the structures are also gathered in Table 2.

Table 2. ESI-MS and LIFDI-MS analysis of the reaction of 3 with NaNO3 in AcOH at 50 °C at 1 h.a

|  |  |
| --- | --- |
| Key ion observed by ESI-MS | Key ion observed by LIFDI-MS |
|  |  |

a The structures are suggested for key molecular ion peaks observed by ESI-MS and LIFDI (**I** = [C22H22N3O5Pd2Na]+ and **I'** = [C22H22N3O5Pd2]•+ and – it is feasible that the methoxy/NO3 ions could occupy different positions, and offer bridging or terminal coordination to Pd.

A radical cation **I'** was observed by LIFDI-MS, which provides support for these higher oxidation state Pd species, containing a nitrate ligand. At 1.5 h, other ions were observed, including a partially oxidized dinuclear Pd species by ESI-MS, which supports the formation of complex **9** underworking reaction conditions and consistent with the NMR studies (see Supporting Information). After 2 h, the major ions observed by ESI-MS and LIFDI-MS were derived from **9**. Other ions were detected under the working reaction conditions, for which attempts to fit reasonable structures and chemical formulae were unsuccessful.

**Reaction kinetics and appearance of gases under working catalyst conditions.** The originally reported reaction of **1**→**2**, mediated by Pd(OAc)2 and 1 eq. NaNO3, in air-saturated AcOH, was conducted for 18 h at 110 °C (Fig. 11).3 We learnt that this reaction was over within minutes at this temperature. Lowering the reaction temperature to 80 °C allowed the evolution of product **2** to be monitored by GC analysis (temp. at *t* = 0 min was 80 °C). In all cases classical homogeneous behavior is apparent and there is no evidence to suggest the involvement of Pd nanoparticles (heterogeneous processes) under these oxidizing conditions.[[33]](#endnote-33) The reaction mediated by Pd(OAc)2 reaches 94% conversion after 10 min. The catalytic competency of the presynthesized complexes **3**, **7a**, **7b**, **8** and **9** was established under otherwise identical conditions to Pd(OAc)2. It is apparent that the kinetics observed for the reaction mediated by Pd(OAc)2 is different to that mediated by **9**. The appearance of a defined induction period suggests that **9** is a pre-catalyst. The initially formed palladacycle **3** and *trans-*Pd(OAc)2(**2**)­2 **8** share catalytic activity that is commensurate with Pd(OAc)2. Within the series the most active catalyst was **7b**, containing an NO2 anion, which was found more active that the corresponding catalyst **7a**, containing an NO3 anion.

**Fig. 11** Kinetic plots for the reaction of **1**→**2** catalyzed by Pd(OAc)2 (5 mol% Pd), and complexes **3**, **7a**, **7b**, **8** and **9** (1 eq. of NaNO3, 80 °C, air-saturated AcOH). Reactions with dinuclear Pd complexes employed 10mol% Pd. Each data point is an average of three independent GC injections (error bars for each conversion point are shown against each curve).

In reactions of **1**, mediated by Pd(OAc)2 in the presence of 1 equiv. of NaNO3, the evolution of NO is seen on heating between 80-110 °C. The appearance of a red / brown gas is visible after ~2 min reaction time which is attributed to NO2↑ *vide infra*. Infrared spectroscopic analysis of the catalytic reaction **1** → **2** under working conditions at 80 °C (under air) revealed that two new bands at 2213 and 2178 cm-1 grew in after 2 h reaction time (see Supporting Information). These bands were attributed to N2O,[[34]](#endnote-34) the formation of which occurs on full consumption of substrate **1**.

Gas head-space analysis, using a customized chemiluminescence NOx analyzer (see experimental section), of the reaction of **1 → 2** catalyzedby Pd(OAc)2 in the presence of 1 eq. NaNO3, allowed the gases evolved to be characterized. It was necessary to run a reaction using 2.3 mmol of **1** in AcOH/Ac2O (40 mL, 7/1, v/v), giving a concentration in **1** of 0.0575 M. The gases were analyzed directly from the top of the reaction condenser, equipped with a glass tubing-based piece allowing the entrance of a flux of “zero-air” and the exit of the gases to the detectors. The volume dilution was 15 L min-1. The reaction was started at 25 °C, as the large volume of AcOH/Ac2O would require *ca.* 20 min to reach 110 °C. The experiment conducted in this way showed that mixing **1**, Pd(OAc)2 and NaNO3 in AcOH/Ac2Oled to the evolution of NOx gases at 25 °C (depicted as product evolution curves in Fig. 12).The concentrations of NOx gases reported are given as mixing ratios, in parts per million. The total amount of NOx formed is *ca.* 140 ppm (~1.2 mmol), consuming over half of the NaNO3 (2.3 mmol) initially present. The experiment confirms that NO is formed rapidly under these reactions. NO2 also forms, which continues to increase at the expense of NO; therefore, as demonstrated by this experiment, air (O2) is playing the role of reoxidant.

The interaction of nitrate with air in light could also lead to the formation of O3. However, there was no clear evidence that light affected the catalytic chemistry (*cf.* only a marginal difference in acetoxylation reaction kinetics was recorded). Moreover, the formation of O3 was not detected under these reaction conditions.

Following on from the results gained by the head-space analysis, we tested the reaction **1** → **2**, mediated by Pd(OAc)2 (5 mol%) and NaNO3 (1 eq.) in AcOH at room temperature, which gave **2** in 90% conversion after 3 days.

A preparative scale reaction of **2**, catalyzed by 5 mol% Pd(OAc)2, 1 equiv. NaNO3 in AcOH/Ac2O at 110 °C, gave liberated acid **10** in 23% yield (Fig. 13). Future studies will address the feasibility of this catalytic transformation in more general terms, *e.g.* in terms of substrate scope, as it has the potential to be synthetically useful.



**Fig. 12** Head–space analysis of the reaction **1** → **2**, mediated by Pd(OAc)2 (5 mol%) and NaNO3 (1 eq.) in AcOH/Ac2O (*t0 =* 25 °C), with heating to 110 °C (over 15 min) (note: NOx = NO+NO2).

Lastly, reaction of **7b** with NO2 gas was conducted as, based on literature precedent,[[35]](#endnote-35) we envisaged that the NO2 ligand at PdII could be oxidized to NO3(Fig. 14).

**Fig. 13.** Example demonstrating the feasibility of a catalytic reaction **2** → **10**.



**Fig. 14.** Reaction of **7b** with NO2 (gas) monitored by in situ infrared spectroscopic analysis (ReactIRTM) – tentatively suggested oxidized Pd complexes.

Bubbling a CH2Cl2 solution of **7b** with NO2 led to loss of CH3CN from **7b**. Reaction monitoring by *in situ* spectroscopic analysis allowed us to visualize solubilization of NO2(g) (sat. at *ca.* *t*=5 mins), loss of **7b** and formation of a new compound (Fig. 15). On the basis of the IR data, a dinuclear Pd complex possessing two μ-1,3-NO3 ligands (**7aa**)is tentatively proposed, based on a characteristic deformation mode at 717 cm-1, assigned to μ-1,3-NO3, similar to a related complex reported by Yu *et al.* (766 cm-1).21 Extensive analysis by LIFDI was unable to reveal the molecular ion of **7aa**, although a very weak molecular ion for **7ab** was found (see Supporting Information). The 1H NMR spectra of this complex suggests that the quinoline protons have become highly deshielded (distinct from nitrated organic product **11**), in-keeping with the structure proposed containing NO3 anions.



**Fig. 15** The *in situ* IR reaction monitoring of **7b** → **7aa**, in the presence of NO2(g) (1251 cm-1), at 20 °C. The black dots show depletion of **7b** at 1223 cm-1 and red dots show appearance of **7aa** at 717 cm-1.

Discussion and Conclusion

From this study evidence supporting the role of nitrate and nitrite anions at Pd, in the aerobic Pd-catalyzed oxidation of non-activated sp3-C–H bonds, has been gathered. 8-Methylquinoline **1** was identified as a model substrate to conduct this study, which affords acetoxylated product **2**, and was originally reported in Sanford’s work3 as part of an expanded substrate scoping study.

The findings include (all catalytic processes refer to the reaction of **1** → **2** conducted at 110 °C in AcOH/Ac2O, unless specified):

1. Cyclopalladation of **1** with Pd(OAc)2 affords a dinuclear Pd complex **3** (in AcOH), which is catalytically competent.
2. Palladacycles containing NO3 and NO2 ligands (**7a** and **7b** respectively) are both viable (pre)catalysts.
3. Palladacycle **7a** functions as an active catalyst in the absence of additional NaNO3 co-catalyst.
4. Under either N2 or air, a catalytic reaction mediated by 1 equiv. of NaN18O3 showed incorporation of the 18O label into acetoxylated product **2** (in AcOH).Negligible 18O incorporation was recorded under O2.
5. Stoichiometric reactions of **3** with NaNO3 at either 50 or 80 °C revealed the intermediacy of several species – *trans-*Pd(OAc)2(**2**)­2 (**8**) and the oxidized Pd complex **9** could be characterized (in AcOH-*d*4). The latter complex formed quantitatively, after overnight heating at 80 °C.
6. Another intermediate from (e) was revealed by stoichiometric reaction of **3** with Na15NO3, proposed as being a Pd-containing species possessing a NOx ligand.
7. The formation of nitrated product **11** has been observed in stoichiometric reactions of **3** and NaNO3 in acetic acid, which is converted to acetoxylation product **2**, in the presence of Pd at 50 °C, and in the absence of Pd at 110 °C.
8. ESI-MS and LIFDI-MS provided indirect evidence for the formation of dinuclear palladacycles containing NO3 anion (with AcOH/MeOH), which also confirmed the evolution of an oxidized ligand backbone (leading to the isolation of **9**).
9. Complex **9** is catalytically competent and exhibits an induction period, contrasting with the catalytic behavior of the other Pd complexes (**3**, **7a**, **7b** and **8**).
10. The *in situ* infrared spectroscopic analysis of a catalytic reaction catalyzed by Pd(OAc)2 at 80 °C showed the evolution of N2O, after prolonged heating (up to 12 h).
11. Head-space analysis of a catalytic reaction, started at 25 °C and heated to 110 °C, revealed the rapid formation of NO and NO2 gases within 2 min. The formation of NO and subsequent oxidation to NO2, confirms that NO is being oxidized under the aerobic reaction conditions.
12. The mechanistic observations made above allowed identification of a room temperature catalytic reaction (90% conv. to **2**, over 3 days, was recorded).

Based on the above evidence, a catalytic cycle involving dinuclear palladacycle **3** as an entry point is plausible. The precise redox chemistry involving NO3 and NO2 anions at Pd is undoubtedly complicated. Direct evidence for NO3 and NO2 anions acting as ligands at PdII has been obtained (by X-ray diffraction, NMR spectroscopic and MS analysis). Transfer (exchange) of 18O from NaN18O3 into the acetoxylation product **2** confirms that 18O exchange between NO3 and OAc anions occurs at Pd, which is in-keeping with the observations made by Bäckvall and co-workers in the acetoxylation/hydration reactions of olefins.15

The presence of nitrated product **11** indicates that NO2 is acting as a ligand at Pd and that reductive elimination is feasible. Moreover, such products are intermediates to acetoxylated product **2**.

The formation of complex **9** indicates that the reaction of **1** → **2** is running under strongly oxidizing conditions. Prolonged heating will therefore lead to loss of product **2**, impacting on overall yield. The primary reason for this is that *trans-*Pd(OAc)2(**2**)­2 (**8**) goes on to form complex **9**, under the reaction conditions.

NOx gases readily evolve in the aerobic Pd-catalyzed oxidation of non-activated sp3-C–H bonds.3 Our head-space measurements indicate that NO is rapidly formed under working reaction conditions, starting measurements at room temperature. We believe that the solubility of NaNO3 is critical here, where higher temperatures favor dissolution.

Oxidation of Pd-NO species to Pd-NO2 and Pd-NO3 species is reported,[[36]](#endnote-36) and there is an interesting complementarity here with iron-nitrato/iron-nitrosyl chemistry.[[37]](#endnote-37),16b

The formation of N2O is noted on prolonged heating and reaction times (by *in situ* IR measurements). We cannot identify a clear role for N2O, other than it is a dead-end for catalysis, which is in-keeping with the timing of its appearance, long after substrate turnover has completed. N2O formation can be explained by dimerization of HNO as a termination reaction.[[38]](#endnote-38)

We propose a mechanism involving higher oxidation state Pd species (Fig. 16). It is unclear whether PdIV species are involved in these transformations – with the experimental evidence available we propose that dinuclear PdIII species play an important role in catalysis, which is based on the combined NMR, MS and IR data that we have available from this study. The mechanism makes the reasonable assumption that Pd3(OAc)6 breaks down to form ‘Pd(OAc)2’ under the reaction conditions. The caveat to our hypothesis is that structurally characterized PdIV species containing NO, NO2 and NO3, containing tris(pyrazolyl)borate ligands have been reported by Cámpora and co-workers.[[39]](#endnote-39) These model systems are of potential relevance to the catalytic C-H acetoxylation reaction mechanism, particularly as oxygen was shown to oxidize a ‘PdIV-NO’ complex to ‘PdIV-NO3’.

 **Fig. 16** Postulated mechanism based on the experimental evidence gathered in this study (where O^O is shown as acetate, the bridging ligand could also be nitrate).

Cyclopalladation can occur through either monomer or dimer complexes (step 1 and step 5), a proposal supported by Musaev’s recent study.[[40]](#endnote-40) NO2–/NO3– metathesis is facile at Pd, as demonstrated by experiment (step 2). Species **II** can either react with liberated NO2 to give **III** or directly form **11** by reductive elimination (indicated as step 12). **III** can then be directly oxidized under the reaction conditions to give **IV** (step 7), a species speculated by Liu and co-workers as being formed in reactions employing *tert*-butyl nitrite.[[41]](#endnote-41) The experimental evidence, particularly the 15N NMR evidence, tentatively supports such type of an intermediate being formed under the reaction conditions. Intermediate **IV** can also derive from NO2 oxidation of validated dimer intermediate **3** (step 7). It is further recognized that NOx-free intermediates could form under the conditions, either by oxidation of **3** (step 6) or anion metathesis with **IV** (step 8), giving **V**. Against this latter proposal is the 18O-labeling studies indicating that NOx is at Pd for oxygen exchange to occur intramolecularly with acetate (18O appearing in product **2**). Reductive elimination from **V** gives acetoxylated product **2** (step 9) and a Pd species that requires reoxidation to ‘Pd(OAc)2’ (step 10), which is feasible under the oxidizing conditions of the reaction. The nitrated organic product **11** can form directly from **IV**, in keeping with that proposed.38 Here, a Pd reoxidation step is again necessary, akin to step 10 (not shown). Step 11 shows how nitrated organic product **11** can be converted into **2**, confirmed by experiment as being more rapid in the presence of Pd, although it occurs without.

We regularly encountered formation of complex **9** in our studies, which can derive from **IV** by oxidation of the methylene group to a carbonyl (step 13). The characterization of the potential intermediate **12**, from the 15N NMR labeling studies, provides support for this hypothesis – the very high chemical shift for a methylene proton (δ 8.29 ppm) indicates an interaction of an NOx anion (at Pd), which can ultimately assist this oxidation step.

To conclude, the principal aim of this investigation was to delineate the role played by nitrate and nitrite anions in the aerobic Pd-catalyzed oxidation of non-activated sp3-C–H bonds. Here, we were able to draw on the promising methodology described by Sanford,3 and other Pd-catalyzed processes taking advantage of such redox anions.8,9 Recent synthetic developments,5,7 when taken together with the mechanistic work described herein, serve to highlight the potential of redox active anions such as nitrate and nitrite in oxidative Pd-catalyzed processes. The approach taken to testing the catalytic viability of suitable ‘Pd-NOx’ complexes will, we hope, be more widely adopted by others in studying Pd/NOx–mediated organic transformations, which may also prove useful in understanding regiochemical consequences in appropriate transformations. The intimate role of NOx at Pd is undoubtedly complicated, but through appropriate isotopic labeling and complementary mechanistic studies, useful experimental evidence can be gathered.

Experimental Section

**General Experimental and Instrumental details.** Reagents were purchased from Sigma-Aldrich, Alfa Aesar, Acros Organics or Fluorochem and used as received unless otherwise stated. Isotopically labeled chemicals were purchased from Icon Isotopes Ltd. and used as received. Pd(OAc)2 was obtained from Precious Metals Online. Dry THF, CH2Cl2 and CH3CN were obtained from a Pure Solv MD-7 solvent system and stored under nitrogen. THF was also degassed by bubbling nitrogen through the solvent with sonication. Dry methanol was obtained by drying over 3 Å molecular sieves. Petroleum ether refers to the fraction of petroleum that is collected at 40-60 °C. Reactions requiring anhydrous conditions were carried out using Schlenk techniques (high vacuum, liquid nitrogen trap on a standard in-house built dual line). Room temperature upper and lower limits are stated as 13-25 °C, but typically 21 °C was recorded. Brine refers to a saturated aqueous solution of NaCl.

Thin layer chromatography (TLC) was carried out using Merck 5554 aluminum backed silica plates (silica gel 60 F254) and spots were visualized using UV light (at 254 nm). Where necessary, plates were stained and heated with one of potassium permanganate, anisaldehyde or vanillin as appropriate. Retention factors (Rf) are reported in parentheses along with the solvent system used. Flash column chromatography was performed according to the method reported by W. C. Still *et al.*[[42]](#endnote-42) using Merck 60 silica gel (particle size 40–63 μm) and a solvent system as reported in the text.

NMR spectra were obtained in the solvent indicated, using a JEOL ECX400 or JEOL ECS400 spectrometer (400MHz, 101 MHz and 162 MHz for 1H, 13C and 31P, respectively), or a Bruker 500 (500 MHz, 126 MHz and 202 MHz for 1H, 13C and 31P, respectively). Chemical shifts are reported in parts per million and were referenced to the residual non-deuterated solvent of the deuterated solvent used (CHCl3 TMH = 7.26 and TMC = 77.16 (CDCl3), CDHCl2 TMH = 5.31 and TMC = 54.0 (CD2Cl2), (CHD2)SO(CD3) TMH = 2.50 and TMC = 39.52 {SO(CD3)2}, 1H and 13C respectively). AcOD-d3 was referenced to 2.04 ppm (1H only). Spectra were typically run at a temperature of 298 K. All 13C NMR spectra were obtained with 1H decoupling. 31P NMR were referenced internally, and recorded with 1H decoupling. NMR spectra were processed using MestrNova software (versions 5.3, 7.03 and 8.1). The spectra given below were usually saved as .emf files in MestrNova and inserted into a Microsoft Word Document. For the 1H NMR spectra the resolution varies from 0.15 to 0.5 Hz; the coupling constants have been quoted to ± 0.5 Hz in all cases for consistency. 1H NMR chemical shifts are quoted to 2 decimal places; 13C and 31P NMR chemical shifts are quoted to 1 decimal place (note: for some 13C signals it was necessary to quote 2 decimal places).

High-field NMR spectra were acquired at 16.4 T on a Bruker Avance II spectrometer equipped with 5mm TXI or BBO probes. Spectra of natural abundance samples (**1**, **2**, **3**, **7b**, **10** and **9**) and the monitoring of the reaction of **3** to **2** were acquired using the TXI probe. The monitoring of the reaction of **1** to **2** in the presence of Na15NO3 was performed with the BBO probe to facilitate direct observation of 15N species. 1H NMR spectra (700.13 MHz) were acquired using a Bloch-decay (single-pulse) sequence with a 5 s recycle delay, 15 ppm spectral widths, 3 second acquisition times are the sum of 32 co-added transients. 1H{15N} correlation spectra (700.13 and 70.96 MHz, respectively) were acquired using an HMQC pulse sequence with pulsed field-gradient based coherence selection. Spectra were acquired with different spectral widths and/or transmitter offsets in the 15N dimension in order to ensure detect for possible leasing of signals in the indirect dimension. 1H chemical shifts are reported relative to TMS, and 15N chemical shifts are reported relative to liquid ammonia.

Infrared spectra were obtained using either a Unicam Research Series FTIR (KBr IR) or a Bruker ALPHA-Platinum FTIR Spectrometer with a platinum-diamond ATR sampling module. Where indicated, reactions were monitored in situ using a Mettler Toledo ReactIR ic10 with a K6 conduit SiComp (silicon) probe and MCT detector.

MS spectra were measured using a Bruker Daltronics micrOTOF MS, Agilent series 1200LC with electrospray ionization (ESI and APCI) or on a Thermo LCQ using electrospray ionization, with <5 ppm error recorded for all HRMS samples. LIFDI mass spectrometry was carried out using a Waters GCT Premier MS Agilent 7890A GC (usually for analysis of organometallic compounds when ESI or APCI are not satisfactory ionization methods). Mass spectral data is quoted as the m/z ratio along with the relative peak height in brackets (base peak = 100). Mass to charge ratios (*m/z*) are reported in Daltons. High resolution mass spectra are reported with <5 ppm error (ESI) or <20 ppm error (LIFDI). For clarity, LIFDI data are reported for 106Pd, the most abundant natural isotope of Pd.

Melting points were recorded using a Stuart digital SMP3 machine.

Gas chromatographic analysis was carried out using a Varian CP-3800 GC equipped with a CP-8400 autosampler. Separation was achieved using a DB-1 column (30 m × 0.32 mm, 0.25 μm film thickness) with carrier gas flow rate of 2 mL min-1 and a temperature ramp from 50 to 250 °C at 20 °C min-1. The injection volume was 1 μL with a split ratio of 10 (details of the kinetics measurements are given below).

The chemiluminescence NOx analyzer is a custom dual channel instrument from Air Quality Design (AQD inc. Golden, Colorado) measuring at 1 Hz on both channels simultaneously. Channel 1 (ch1) measures NO and has a nominal sensitivity of 3.5 counts per second / parts per trillion (cps/ppt). Channel 2 (ch2) measures NOx (NO + NO2) by dissociating NO2 to NO with a photolytic converter (blue light converter) that irradiates the sample gas at 390 nm. The nominal sensitivity on channel 2 is 4 cps/ppt. NO2 is obtained by subtracting ch1 from ch2. The effective limit of detection is ~ 2.5 ppt/minute NO and ~ 6.5 ppt/minute NO2. Note: ppm values are given in Fig, 12. Pre-chamber zero measurements are taken every 5 minutes for 30 seconds. The whole system is kept at 4 torr vacuum pressure. The sample flow rate is 1sLpm per channel - MFC controlled. Calibration for sensitivity is done by standard addition of NO; converter efficiency is determined by gas phase titration (GPT) of NO to NO2 with O3. Artefact is determined in zero air, which is made by taking dried (-40 °C dew point) compressed air, passing it through 13x molecular sieves, then sofonofil to remove NOx and through activated carbon to remove ozone and VOCs. The 2B Technologies Model 202 Ozone Monitor™ is designed to enable accurate and precise measurements of O3 ranging from low ppb (precision of ~1 ppb) up to 100,000 ppb (0-100 ppm) based on the absorption of UV light at 254 nm.

All DFT calculations were performed using the TURBOMOLE V5 package using the resolution of identity (RI) approximation.[[43]](#endnote-43) Initial optimizations were performed at the (RI-)BP86/SV(P) level, followed by frequency calculations at the same level. All minima were confirmed as such by the absence of imaginary frequencies, energies, geometries and vibrational frequencies are presented. Single-point calculations on the (RI)BP86/SV(P) optimized geometries were performed using the hybrid PBE0 functional and the flexible def2-TZVPP basis set. The (RI)PBE0/def2-TZVPP SCF energies were corrected for their zero point energies, thermal energies (∆E) and entropies (obtained from the (RI-)BP86/SV(P)-level frequency calculations at 298.15K, ∆G298.15). In all calculations, a 28 electron quasi-relativistic ECP replaced the core electrons of Pd. No symmetry constraints were applied during optimizations. Calculated XYZ coordinates, single point energies and vibrational spectra are reported in the supplementary information.

**Characterization of Pd complexes**

**Dinuclear PdII-PdII complex 3 {Pd(8-MQ)(OAc) dimer}.** 8-Methylquinoline (186 mg, 1.3 mmol) and Pd(OAc)2 (291 mg, 1.3 mmol) were suspended in glacial acetic acid (20 mL), refluxed for 1.5 h and then filtered. Water (150 mL) was added to the filtrate and the mixture left overnight. The precipitated product was collected by filtration and recrystallized from CH2Cl2/hexane to yield **3** as a bright orange solid as a 2:1 mixture of isomers (342 mg, 85 % yield). Crystals suitable for X-ray diffraction were grown by layering of a CH2Cl2 solution with pentane. Mp 193-195 °C; 1H NMR (Major isomer)(400 MHz, CDCl3) δ 8.51 (dd, *J* = 5.0, 1.5 Hz, 2H, H2), 7.87 (dd, *J* = 8.4, 1.5 Hz, 2H, H4), 7.22 (dd, *J* = 8.3, 5.0 Hz, 2H, H3), 7.11-6.99 (m, 2H, H5), 6.89 (dd, *J* = 8.1, 7.1 Hz, 2H, H6), 6.70 (dd, *J* = 7.1, 1.1 Hz, 2H, H7), 3.45 (d, *J* = 13.8 Hz, 2H, CH2), 2.55 (d, *J* = 13.8 Hz, 2H, CH2), 2.14 (s, 6H, CH3); 13C NMR (101 MHz, CDCl3) δ 181.5 (CO), 152.7 (C9), 148.9 (C2), 148.2 (C10), 136.5 (C4), 127.3 (C6), 126.8 (C7), 122.9 (C5), 121.1 (C3), 120.5 (C8), 41.4 (CH2), 24.5 (CH3); LIFDI-MS m/z 615.94 (Calc. for C24H22N2O4Pd2 615.97); ESI-MS m/z 614.9621 (Calc. for C24H21N2O4Pd2 ([M-H]+) 614.9620; IR (KBr, cm-1) 3390, 1566, 1504, 1408, 1050, 817, 776, 671; Anal. calc. for C24H22N2O4Pd2 C 46.85, H 3.60, N 4.55, observed low C (46.17), H 3.59, N 4.48.

**Dinuclear PdII-PdII complex 4 {Pd(8-MQ)(Cl) dimer}.** To a solution of **3** (265 mg, 0.43 mmol) in acetone (15 mL) was added lithium chloride (73 mg, 1.72 mmol) in distillated water (10 mL), resulting in immediate precipitation of the product. The precipitate was collected by filtration and washed with methanol/water (1:1 v/v) to yield **4** as a pale yellow powder (195 mg, 80% yield). Pyridine-*d*5 was added to an NMR tube containing a sample of complex **4** in CDCl3, in order to increase its solubility in common NMR solvents. Upon addition of pyridine-*d*5, a yellow solution was formed, presumably due to the formation of the monomeric complex [PdCl(8-MQ)(pyr-*d*5)]. Residual pyridine signals have been omitted from the reported NMR data for clarity. Mp 249-251 °C; 1H NMR (400 MHz, CDCl3) δ 9.57 (dd, *J* = 5.1, 1.5 Hz, 2H, H2), 8.10 (dd, *J* = 8.3, 1.5 Hz, 2H, H4), 7.54-7.50 (m, 2H, H5) 7.47-7.42 (m, 2H, H7), 7.38 (dd, *J* = 7.3, 7.0 Hz, 2 H, H6), 7.31 (dd, *J* = 5.1, 8.3 Hz, 2H, H3) 3.54 (s, 4H, CH2); 13C NMR (101 MHz, CDCl3) δ 153.1 (C9), 151.8 (C10), 147.3 (C8), 137.2 (C4), 128.7 (C5), 127.8 (C6), 127.6 (C7), 123.5 (C2), 121.2 (C3), 30.1 (CH2); LIFDI-MS m/z 567.90 (Calc. for C20H16Cl2N2Pd2 567.88); IR (KBr, cm-1) 3059, 2919, 2283, 1563, 1505, 1385, 1375, 1316, 1056, 825, 787, 762, 676; Anal. calc. for C20H16Cl2N2Pd2 C 42.28, H 2.84, N 4.93, observed C 41.92, H 2.65, N 4.71.

**Mononuclear PdII complex 5 {Pd(8-MQ)(PPh3)Cl}.** A solution of Pd(8-MQ)(Cl**)** dimer **4** (290 mg, 0.5 mmol) and PPh3(288 mg, 1.1 mmol) in CH2Cl2 (20 mL) was stirred at room temperature for 15 min under nitrogen. The reaction mixture was filtered through CeliteTM and hexane was added to induce precipitation. The product was collected by filtration and recrystallized from CH2Cl2/hexane to yield **5** as fine yellow crystals in quantitative yield (579 mg). Mp 205-209 °C; 1H NMR (400 MHz, CDCl3) δ 9.79 (m, 1H, H2), 8.27 (dd, *J* = 8.3, 1.6 Hz, 1H, H4), 7.86-7.77 (m, 6H, Ar-H), 7.58 (d, *J* = 7.9 Hz, 1H, H5 or H7), 7.52 (ddd, *J* = 8.3, 5.0, 1.2 Hz, 1H, H3), 7.46-7.39 (m, 9H, Ar-H), 7.39-7.36 (m, 1H, H6), 7.29 (dq, *J* = 7.2, 1.3 Hz, 1H, H5 or H7), 2.85 (d, *J* = 3.8, 2H); 13C NMR (101 MHz, CDCl3) δ 152.2, 150.4, 148.2, 137.9, 135.0 (d, *J* = 11.9 Hz), 131.6, 131.1, 130.5 (d, *J* = 2.6 Hz), 129.1, 128.4 (d, *J* = 10.8 Hz), 127.7, 123.8, 121.6, 33.4; 31P NMR (162 MHz, CDCl3) δ 35.2; LIFDI-MS m/z 545.05 (Calc. for C28H23ClNPPd 545.03); Anal. calc. for C28H23ClNPPd C 61.56, H 4.24, N 2.56, observed C 61.70, H 4.12, N 2.21.

**Mononuclear PdII complex 6a {Pd(8-MQ)(NO3)(PPh3)}.** A solution of **5** (250 mg, 0.46 mmol) and silver nitrate (389 mg, 2.29 mmol) in CH2Cl2 (20 mL) was stirred at room temperature for 24 h. The reaction mixture was filtered and the filtrate concentrated in vacuo to yield **6a** as a pale yellow solid in quantitative yield (280 mg). Crystals suitable for X-ray diffraction were grown by layering of a CH2Cl2 solution with cyclohexane. Mp 180-183 °C; 1H NMR (400 MHz, CD2Cl2) δ 8.75-8.71 (m, 1H, H2), 8.39 (dd, *J* = 8.3, 1.2 Hz, 1H), 7.77-7.64 (m, 3H), 7.55-7.36 (m, 16H), 3.04 (d, *J* = 4.2 Hz, 2H); 13C NMR (101 MHz, CD2Cl2) δ 151.1, 148.8, 147.7, 138.4, 134.2 (d, *J* = 11.9), 133.9 (d, *J* = 16.0 Hz), 130.9 (d, *J* = 2.5 Hz), 129.2, 128.8, 128.7 (d, *J* = 11.0 Hz), 128.0, 124.1, 121.8, 26.8; 31P NMR (162 MHz, CD2Cl2) δ 33.0; LIFDI-MS m/z 510.04 [M−NO3] (Calc. for C28H23NPPd 510.06); IR (KBr, cm-1) 3054, 1505, 1447, 1384, 1286, 1096, 1021, 825, 786, 751, 696.

**Mononuclear PdII complex 6b {Pd(8-MQ)(NO2)(PPh3)}.** A solution of **5** (250 mg, 0.46 mmol) and silver nitrite (352 mg, 2.29 mmol) in CH2Cl2 (20 mL) was stirred at room temperature for 24 h. The reaction mixture was filtered and the filtrate concentrated in vacuo to yield **6b** as a light brown solid in quantitative yield (315 mg). We noted that complex **6b** is sensitive to air and moisture (OPPh3 formed over time in CDCl3 solutions of **6b**). Mp 178-180 °C; 1H NMR (400 MHz, CD2Cl2) δ 8.68 (s, 1H), 8.35 (d, J = 8.2 Hz, 1H), 7.77-7.68 (m, 5H), 7.51-7.37 (m, 12H), 7.36-7.30 (m, 1H), 2.72 (s, 2H); 31P NMR (162 MHz, dry CD2Cl2) δ 32.4; LIFDI-MS m/z 510.03 [M−NO2] (Calc. for C28H23NPPd 510.06); IR (KBr, cm-1) 3055, 2870, 1684, 1569, 1503, 1481, 1431, 1340, 1095, 825, 752, 696. Complex **6b** retained 0.25 equivalents of AgCl. Further purification led to its decomposition (we were unable to obtain a satisfactory 13C NMR data for **6b**). Anal. calc. for C28H23N2O2PPd·Ag0.25Cl0.25 C 56.74, H 3.91, N 4.73, observed C 56.77, H 3.95, N 4.68 (average of 2 runs).

**Mononuclear Pd(II) complex 7a {Pd(8-MQ)(NO3)(NCCH3)}.** Complex **4** (140 mg, 0.25 mmol) and silver nitrate (100 mg, 0.6 mmol) were suspended in a mixture of CH2Cl2 and CH3CN (8 mL, 3:1 v/v) and stirred at room temperature for 24 h. The reaction mixture was filtered and the filtrate concentrated in vacuo to yield **7a** as a brown solid in quantitative yield (228 mg). Mp 139-143 °C; 1H NMR (400 MHz, CDCl3) δ 8.64 (dd, *J* = 5.2, 1.5 Hz, 1H, H2), 8.26 (dd, *J* = 8.4, 1.5 Hz, 1H, H4), 7.59 (dd, *J* = 7.8, 1.3 Hz, 1H, H5), 7.53 (dq, *J* = 7.1, 1.3 Hz, 1H, H7), 7.46 (dd, *J* = 7.1, 7.8, Hz, 1H, H6), 7.40 (dd, *J* = 5.2, 8.4 Hz, 1H, H3) 3.69 (s, 2H, CH2), 2.34 (s, 3H, CH3); 13C NMR (101 MHz, CDCl3) δ 152.5 (C2), 149.7 (C9), 146.5 (C8), 138.4 (C4), 129.0 (C6), 128.5 (C7), 128.3 (C5), 124.2 (C3), 121.7 (CN), 23.0 (CH2), 3.6 (CH3); LIFDl-MS m/z 309.98 [M−NCCH3] (Calc. for C10H8N2O3Pd 309.96); IR (KBr, cm-1) 2924, 2853, 2253, 1732, 1508, 1438, 1384, 1290, 1027, 824, 783, 327.

**Mononuclear PdII complex 7b {Pd(8-MQ)(NO2) (NCCH3)}.** Method A - starting from **4** and AgNO2: Complex **4** (140 mg, 0.25 mmol) and silver nitrite (91 mg, 0.6 mmol) were suspended in a mixture of CH2Cl2 and CH3CN (8 mL, 3:1 v/v) and stirred at room temperature for 24 h. The reaction mixture was filtered and the filtrate concentrated in vacuo to afford **7b** as a yellow solid in quantitative yield (235 mg). Method B: starting from **3** and NaNO2 – Complex **3** (105 mg, 0.171 mmol) and sodium nitrite (118 mg, 1.710 mmol) were suspended under argon in distilled CH3CN (5 mL) and stirred at reflux for 6 h. The reaction mixture was filtered while hot under argon. Yellow crystals suitable for X-ray diffraction were grown in the filtrate when cooled down. The crystals were isolated by filtration and dried to yield **7b** in 61 % yield (71 mg). Mp 239-242 °C; 1H NMR (400 MHz, CDCl3) δ 8.53 (dd, *J* = 5.0, 1.5 Hz, 1H, H2), 8.29 (dd, *J* = 8.4, 1.5 Hz, 1H, H4), 7.66-7.57 (m, 2H, H5+H7), 7.49 (t, *J* = 7.6 Hz, 1H, H6), 7.43 (dd, *J* = 8.4, 5.0 Hz, 1H, H3), 3.94 (s, 2H), 2.01 (s, 3H); 13C NMR (101 MHz, CDCl3) δ 152.6 (C2), 149.6 (C9), 147.2 (C8), 138.7 (C4), 129.4 (C6), 129.2 (C7), 128.8 (C5), 127.9 (C10), 124.4 (C3), 121.8 (CN), 27.2 (CH2), 2.1 (CH3); LIFDl-MS m/z 589.85 [2M-2CH3CN] (Calc. for C20H16N4O4Pd2 589.93), 389.06 [M−NO2+8-MQ] (Calc. for C20H16N2Pd 390.03); IR (KBr, cm-1) 2919, 2849, 1505, 1435, 1374, 1216, 1055, 1018, 818, 778.

**Mononuclear PdII complex 8.** Method A - starting from **3** and NaNO3: complex **3** (31.7 mg, 0.052 mmol) and NaNO3 (4.4 mg, 0.052 mmol) were suspended in glacial acetic acid (5 mL) and heated at 50 °C for 1 h. The resulting solution was filtered and concentrated under vacuum. Layering a solution of the previous powder dissolved in CH2Cl2 by pentane led to co-crystallization of **8** as orange crystals and **9** as green crystals. Method B – starting from Pd(OAc)2 complex and **2**: Pd(OAc)2 (53.9 mg, 0.24 mmol) and **2** (91 mg, 0.48 mmol) were suspended in distilled CH2Cl2 (5 mL) under argon and mixed at room temperature for 6 hours. The resulting solution was layered by distilled pentane (15 mL) and the flask was left overnight at 4 °C. The precipitate was filtered and dried under vacuum to afford complex **9** as a green-brown powder. Crystals suitable for X-ray diffraction were directly obtained by layering a solution of **9** in CH2Cl2 by pentane. Selected data from a single crystal (from X-ray): 1H NMR (400 MHz, CDCl3) δ 8.96 (dd, *J* = 4.2, 1.7 Hz, 2H, H2), 8.18 (dd, *J* = 8.3, 1.7 Hz, 2H, H4), 7-85-7.75 (m, 4H, H5+H7), 7.55 (dd, *J* = 8.2, 7.1 Hz, 2H, H6), 7.44 (dd, *J* = 8.3, 4.2 Hz, 2H, H3), 5.86 (s, 4H), 2,28 (s, 3H), 2.21 (s, 6H), 1.96 (s, 3H).

**Dinuclear PdII-PdII complex 9.** Method A – starting from **3** and NaNO3: Complex**3** (115 mg, 0.19 mmol) and NaNO3 (16 mg, 0.19 mmol) were suspended in glacial acetic acid (10 mL) and heated at 80 °C for 3 h. The resulting solution was filtered and concentrated under vacuum to afford complex **8** as an orange powder in quantitative yield (134 mg). Method B – starting from Pd(OAc)2 complex and 8-quinoline carboxylic acid **10**: Pd(OAc)2 (104 mg, 0.46 mmol) and 8-quinoline carboxylic acid **10** (80 mg, 0.46 mmol) were suspended in glacial acetic acid (10 mL) and heated at 110 °C for 1.5 h. The resulting solution was filtered and poured into cold distilled water (200 mL). The flask was left overnight at 4 °C. The mixture was concentrated under vacuum to induce precipitation of the product. The precipitate was filtered and dried under vacuum to afford complex **8** as an orange powder with 68 % yield (106 mg). Crystals suitable for X-ray diffraction were directly obtained from the concentrated solution of **8** in AcOD (NMR tube). 1H NMR (400 MHz, CDCl3) δ 8.76 (dd, *J* = 5.5, 1.6 Hz, 2H, H2), 8.46 (dd, *J* = 8.2, 1.6 Hz, 2H, H4), 8.01 (dd, *J* = 7.4, 1.6 Hz, 2H, H5), 7.86 (dd, *J* = 8.1, 1.7 Hz, 2H, H7), 7.58 (dd, *J* = 8.2, 5.5 Hz, 2H, H3), 7.31 (t, *J* = 7.7 Hz, 2H, H6), 2.12 (s, 6H, CH3); 13C NMR (101 MHz, CDCl3) δ 186.2 (CO, Bn), 172.3 (CO, AcO), 166.8 (C10), 154.6 (C2), 141.8 (C4), 138.1 (C5), 132.8 (C7), 129.6 (C6), 127.4 (C3), 123.8 (C8), 122.0 (C9),24.0 (CH3); LIFDI-MS m/z 450.93 (Calc. for C20H12N2O4Pd1 ([M-Pd-2OAc]) 450.99); ESI-MS m/z 698.9075 (Calc. for C24H18N2O8Pd2 ([M+Na]+) 698.9079; IR (ATR, cm-1) 3399, 3064, 1722, 1563, 1416, 1333, 1304, 769, 697.

**Catalytic evaluation of the complexes in the acetoxylation reaction of 1.** General procedure A – acetoxylation of 8-methylquinoline **1** under air: To a microwave flask containing Pd precatalyst (0.0125 mmol, 5 mol% w.r.t. substrate) and NaNO3 (0-1 eq. relative to substrate) was added 2 mL AcOH/Ac2O (7:1). 8-Methylquinoline **1** (34 μL, 0.25 mmol) was added via syringe. The reaction mixture was heated at 110 °C, and the flask was flushed with compressed air at hourly intervals. After heating for 24 h, the reaction mixture was cooled to room temperature, filtered through a plug of CeliteTM, and the solvent removed under reduced pressure. Sodium bicarbonate (saturated solution in water) was added to neutralize the residue, and the organic products were extracted into ethyl acetate. The organic extracts were washed with brine, dried over magnesium sulfate, and concentrated in vacuo. 1H NMR spectroscopic (integration of the CH2 signal) and gas chromatographic analysis of the crude product was used to calculate conversion (tR1 = 6.53 min, tR2 = 9.06 min), and the acetoxylated product **2** was then purified by flash chromatography on silica gel (35% EtOAc in hexane).General Procedure B – acetoxylation of 8-methylquinoline **1** under O2: To a Schlenk tube fitted with a Young’s tap and magnetic stirrer bar was added Pd precatalyst (0.0125 mmol, 5 mol% with respect to substrate) and NaNO3 (0-1 eq. relative to substrate). The flask was attached to a grease-free Schlenk line fitted with Young’s taps and was then evacuated (aspirator vacuum) and backfilled with oxygen three times to achieve 1 atm. of O2. The flask was sealed and heated at 110 °C for 24 h. Reaction work-up followed procedure A, described above.

8-Acetoxymethylquinoline **2**: Known compound.2 Rf 0.22 (EtOAc/hexane, 1:3, v/v); 1H NMR (400 MHz, CDCl3) δ 8.97 (ddd, *J* = 4.2, 1.8, 0.9 Hz, 1H, H2), 8.19 (dt, *J* = 8.3, 1.7 Hz, 1H, H4), 7.85-7.74 (m, 2H, H5+H7), 7.55 (dd, *J* = 8.0, 7.2 Hz, 1H, H6), 7.45 (ddd, *J* = 8.3, 4.2, 0.9 Hz, 1H, H3), 5.86 (s, 2H, CH2), 2.16 (s, 3H, CH3); 13C NMR (101 MHz, CDCl3) δ 171.6 (CO), 150.4 (C2), 146.6 (C9), 136.7 (C4), 134.1 (C8), 129.3 (C6), 128.8 (C7), 126.8 (C5), 124.0 (C10), 121.8 (C3), 63.2 (CH2), 21.6 (CH3); HRMS (ESI+) m/z 202.0872 [M+H]+ (calc. for C12H12NO2 202.0868); IR (ATR, cm-1) 3066, 2925, 1735, 1497, 1365, 1345, 1234, 1065, 1022, 827, 793, 764.

**General protocol for the kinetics study of the complexes in the acetoxylation reaction of 1.** To a round-bottom flask containing either of Pd(OAc)2, **3**, **7a**, **7b**, **8** or **9** (5 mol%, 0.023 mmol) and NaNO3 (1 eq. relative to substrate, 39 mg, 0.460 mmol) was added AcOH/Ac2O (8 mL, 7:1 v/v, air-saturated and pre-heated at 80 °C). 8-Methylquinoline (1 eq., 61 μL, 0.460 mmol) was added via syringe. The reaction mixture was heated at 80 °C. Aliquots (0.1 mL) are taken from the reaction mixture every minute during 20 minutes. Aliquots of the reaction were immediately quenched by addition of 0.5 mL of NH4Cl saturated solution. The acetoxylation product was then extracted with 0.5 mL of ethyl acetate, and filtered through a Pasteur pipette, filled with cotton wool and CeliteTM, into a GC vial containing 1 mL of the mesitylene stock solution (12.4 mmol/L, used as a standard reference for the GC measurements). The GC method consists of 3 separate washes with 3 different solvents between each injection. Each sample was injected 3 times, giving 3 independent values for each time interval. Individual points, within each kinetic curve, represents the average value of these data (errors bars are shown in Fig. 10).

**Protocol for the head space analysis of the acetoxylation reaction catalyzed by Pd(OAc)2.** In a 500 mL round-bottom flask equipped with a condenser was added Pd(OAc)2 (25.8 mg, 0.115 mmol, 0.05 eq.), NaNO3 (195.5 mg, 2.30 mmol, 1 eq.), AcOH/Ac2O (40 mL, 7:1, v/v) and 8-methylquinoline (305 μL, 2.30 mmol, 1 eq.). Before the mixture was heated at 110 °C, the top of the condenser was equipped with a glass tubing-based piece allowing the entrance of a flux of “zero-air” and the exit to the NOx detectors. The volume dilution was 15 L per minute, and concentrations are reported in mixing ratios – in this case, in parts per trillion.

**General procedure for the formation of the over-oxidized product 10 from acetoxylated product 2.** To a microwave flask containing Pd(OAc)2 (0.0181 mmol, 5 mol% relative to **2**) and NaNO3 (1 eq. relative to **2**) was added 8 mL AcOH/Ac2O (7:1). Compound **2** (73 mg, 0.36 mmol) was added. The reaction mixture was stirred at 110 °C for 24 h, cooled to room temperature, filtered through a plug of CeliteTM, and the solvent removed under reduced pressure. CH2Cl2 was added, and the organic phase was extracted three times with 2 M NaCl (in water). The organic phase was dried over MgSO4, filtered and the solvent evaporated under vacuum (to give product **2**). The aqueous phase was acidified with 2 M HCl and extracted three times with ethyl acetate. The organic phase was dried over MgSO4, filtered and the solvent removed under vacuum (product **10**). Due to the difficulty associated with the analysis and quantification of the presence of the over-oxidized product (to give acid compound **10**), both by MS and GC, the proportion of the acetoxylated and acid products are given in terms of yields following purification (in Fig. 13).

ASSOCIATED CONTENT

**Supporting Information**. Additional experimental data, full product characterization details (including NMR spectra), X-ray diffraction data and DFT calculations are supplied. This material is available free of charge via the Internet at http://pubs.acs.org.

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ABBREVIATIONS

AcOH – acetic acid

AcOD – acetic acid-*d*4

Ac2O – acetic anhydride

ESI-MS – Electrospray Ionization Mass Spectrometry

LIFDI-MS – Liquid Injection Field Desorption Ionization Mass Spectrometry

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