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**Edge**

# NO$_2$ anion contamination in Pd(OAc)$_2$. On the synthesis of pure Pd(OAc)$_2$L$_2$ and palladacycles containing NO$_2$ anion: the photocrystallographic identification of a metastable Pd($\eta^1$-ONO)(C^N)PPh$_3$ complex

Somia E. Bajwa,[a] Thomas E. Storr,[a,b] Lauren E. Hatcher,[c] Thomas J. Williams,[a] Christoph G. Baumann,[b] Adrian C. Whitwood,[a] David R. Allan,[d] Simon J. Teat,[e] Paul R. Raithby[c]* and Ian J. S. Fairlamb[a]*

**Pd$_3$(OAc)$_5$NO$_2$, an impurity in "Pd(OAc)$_2$" {formally Pd$_3$(OAc)$_6$}, emerges as a serious issue in the synthesis of pure Pd$^{II}$ complexes derived from Pd(OAc)$_2$, for example in our C-H activation precatalyst, Pd(OAc)$_2$(pip)$_2$ (pip = piperidine). A previous proposal that nitrite anion can be formed by oxidation of CH$_3$CN by metallic Pd and air, leading to cyclo(ortho)palladated complexes containing nitrite anion, *e.g.* Pd(NO$_2$)(C^N)L (C^N = papaverine; L = CH$_3$CN or DMSO) can be explained by Pd$_3$(OAc)$_5$NO$_2$ acting as the nitrite source. Finally, photocrystallographic metastable linkage isomerisation and complete conversion to an oxygen-bound nitrito complex Pd($\eta^1$-ONO)(C^N)PPh$_3$ has been seen.**

Palladium(II) acetate, Pd(OAc)$_2$, is used extensively in synthesis and catalysis, for which high purity[1] material can be important.[2] It is well-established that anionic ligands (pseudohalides, *e.g.* acetate) exert a profound effect in Pd-catalysed cross-coupling reactions involving the activation of both C-X and C-H bonds.[3] In recent years *N*-centred electron-deficient anions have shown remarkable catalytic effects, either as spectator ligands[3b-e] or substrates in their own right (*e.g.* in Pd$^{II}$/Pd$^{IV}$ chemistry).[3f]

In our recent work on the Pd/Cu-mediated direct arylation (catalytic C-H functionalisation) of 2'-deoxyadenosines Pd(OAc)$_2$(pip)$_2$ (pip = piperidine) was identified as an effective precatalyst.[4] The complex is formed by reaction of Pd(OAc)$_2$ with piperidine (2 eq. with respect to Pd) in THF at ambient temperature; indeed other secondary amines may be used to access a variety of Pd(OAc)$_2$(HNR$_2$)$_2$ complexes, which are highly effective precatalysts for Suzuki-Miyaura cross-couplings.[5] In follow-up studies Pd(OAc)$_2$(pip)$_2$ was found to be accompanied by Pd(OAc)(NO$_2$)(pip)$_2$ in a ratio of 2.4:1 (as determined by $^1$H NMR spectroscopy - see E.S.I., and Scheme 1). The appearance of nitrite anion (NO$_2^-$), and the characterisation of Pd-nitrito complexes, is the main subject of this paper.

Both Pd(OAc)$_2$(pip)$_2$ and Pd(OAc)(NO$_2$)(pip)$_2$ complexes are separable (unless specified 'NO$_2$' is bonded through the nitrogen atom to Pd$^{II}$), and their structures have been independently confirmed by LIFDI mass spectrometry, elemental analysis and single crystal X-ray diffraction. The X-ray structures of Pd(OAc)$_2$(pip)$_2$ and Pd(OAc)(NO$_2$)(pip)$_2$ are shown in Fig. 1. The absence of H$_2$O molecules[6] in the unit cell for Pd(OAc)$_2$(pip)$_2$ allows a reliable comparison of the structure. The key bond distances for Pd(OAc)$_2$(pip)$_2$ are Pd-Npip = 2.0560(13) and Pd-O = 2.0093(11). In Pd(OAc)(NO$_2$)(pip)$_2$ both Pd-Npip bonds are elongated by comparison, Pd-Npip = 2.0738(17) and 2.0690(17); the same is true for the Pd-O bond {2.0417(14)}, indicative of a *trans*-NO$_2$ group {Pd-NO$_2$ bond distance is 1.9962(18)}.[7]
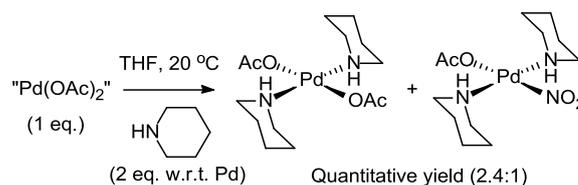


**Scheme 1** PdX$_2$L$_2$ (X = OAc or NO$_2$) complexes derived from Pd(OAc)$_2$, namely Pd(OAc)$_2$(pip)$_2$ and Pd(OAc)(NO$_2$)(pip)$_2$.

After much deliberation regarding the possible sources of nitrite anion,[8] a substantial nitrite impurity was considered most likely. Cotton and Murillo highlighted the non-trivial behaviour of Pd(OAc)$_2$.[9a] This trinuclear 'triangle' complex, formally Pd$_3$(OAc)$_6$, has a nearly idealized $D_{3h}$ symmetry in the solid-state (Fig. 2). In the presence of trace H$_2$O in CDCl$_3$ (*e.g.* laboratory grade CDCl$_3$), Pd$_3$(OAc)$_6$ readily gives Pd$_3$(OAc)$_6$(OH$_2$) (H$_2$O disrupts one bridging acetate group, resulting in desymmetrization). Pd$_3$(OAc)$_6$ is prepared by oxidation of metallic Pd (derived from PdCl$_2$) with HNO$_3$ / AcOH,[10] and as a consequence of poor N$_2$ flow, nitrogen oxides bring about the formation of Pd$_3$(OAc)$_5$NO$_2$.[11] $^1$H NMR spectroscopic analysis of our commercial source of Pd$_3$(OAc)$_6$ in CDCl$_3$ revealed the presence of Pd$_3$(OAc)$_5$NO$_2$ (by comparison with authentic

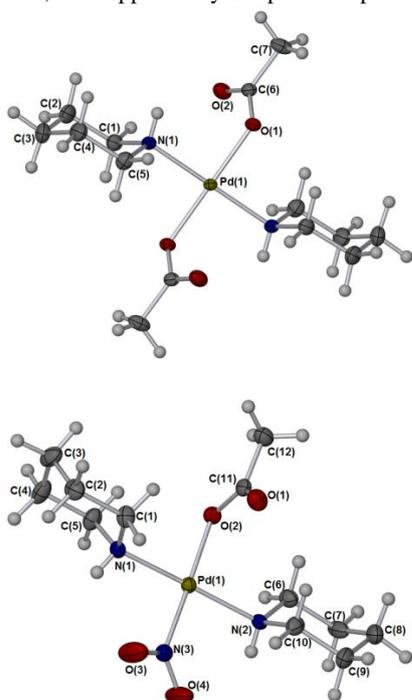material, ~95%, and supported by IR spectroscopic analysis).



**Fig. 1** X-ray structures of Pd(OAc)$_2$(pip)$_2$ (top) and Pd(OAc)(NO$_2$)(pip)$_2$ (bottom).  Thermal ellipsoids set at 50%.
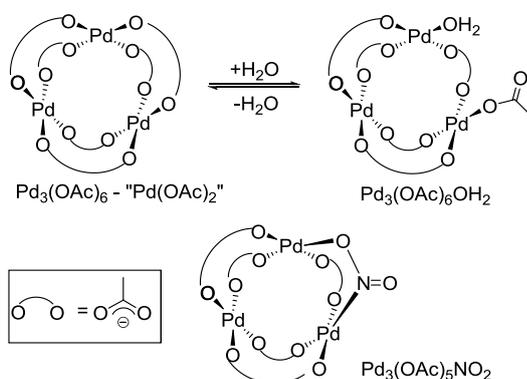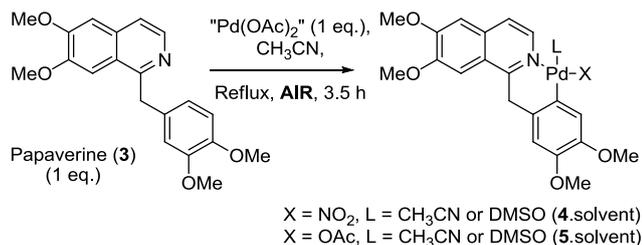


**Fig. 2** Non-trivial behaviour of Pd(OAc)$_2$.[9]

Elemental analysis of the impure commercial Pd(OAc)$_2$ material established the ratio of Pd$_3$(OAc)$_5$NO$_2$:Pd$_3$(OAc)$_6$ as 4.3:1 (81% Pd$_3$(OAc)$_5$NO$_2$; OAc:NO$_2$ ligand ratio = 6.4:1).  The data correlates with the observed Pd(OAc)$_2$(pip)$_2$: Pd(OAc)(NO$_2$)(pip)$_2$ ratio of 2.4:1 from the synthesis (*vide supra*), *e.g.* a ligand ratio of OAc:NO$_2$, *ca.* 5.8:1 (Scheme 1).



**Scheme 2** Orthopalladation of papaverine (**3**).

Other commercial sources of Pd(OAc)$_2$ likely contain nitrite impurities, the question is how much? (see E.S.I. for a comparison of unnamed commercial samples in the Department of Chemistry at York).  In all cases tested nitrite impurities have been identified.[12]

The impact of nitrite impurities from Pd(OAc)$_2$ on catalytic efficacy has not been previously assessed (*e.g.* in Pd-catalysed cross-couplings).[2]  However, given the limited reports of issues with Pd(OAc)$_2$ in catalytic cross-couplings and our early findings[13,14] we suspect that NO$_2$ anion is generally benign, with the caveat that some processes may show differences.  On a general note, this impurity can be missed as Pd(OAc)$_2$ purity is often determined by its total Pd content; 'OAc' and 'NO$_2$' have similar relative molecular masses thus the NO$_2$ impurity is not picked up (*vis-à-vis* Pd$_3$(OAc)$_6$ versus Pd$_3$(OAc)$_5$NO$_2$}.

**Impact of nitrite impurities on the synthesis of pure palladacycles.**

We considered that the NO$_2$ impurities in Pd(OAc)$_2$ could explain observations[15] reported on the synthesis of cyclopalladated nitrito Pd$^{II}$ complexes (*e.g.* **4**·CH$_3$CN and **4**·DMSO, Scheme 2).  It was found that the reaction of Pd(OAc)$_2$ with papaverine **3** in CH$_3$CN at reflux in air for 3.5 h (filtered whilst hot to remove metallic Pd$^0$ residues) gave a filtrate containing **4**·CH$_3$CN, which precipitates out of solution (overnight).  Recrystallization of this precipitate from warm DMSO afforded **4**·DMSO.  The source of nitrite was explained by oxidation of CH$_3$CN mediated by metallic Pd and air (presumably a stoichiometric[16] process), although not proven.

In light of our findings the reaction of papaverine **3** with pure (>99%) Pd$_3$(OAc)$_6$ under air using reagent grade CH$_3$CN (at reflux for 3.5 h) was repeated (several times).[17]  In all cases precipitates were slow to appear (*ca.* 3-14 days at 5 °C),[18] although **3** had been fully consumed (as shown by ^{1}H NMR spectroscopy).  Eventually, a yellow semi-crystalline material appeared which was filtered and analysed.  Elemental analysis and LIFDI mass spectrometric analysis showed this material to have the composition of [Pd(OAc)(C^N)] and not [Pd(NO$_2$)(C^N)].  ^{1}H NMR spectroscopy (in $d_6$-DMSO) revealed that cyclopalladation had occurred, and whilst being similar to the data for **4**·DMSO,[15a] some differences were apparent (*vide infra*).

A series of control reactions with triply distilled CH$_3$CN (from AlCl$_3$, Li$_2$CO$_3$ and CaH), in both the presence and absence of air, gave the same product as detailed above.  In the absence of DMSO the product formed was suspected to be **5**·CH$_3$CN. But crystallisation from CH$_3$CN actually gave a novel dimeric Pd$^{II}$ acetate bridged complex **6** (representative of the bulk material).  The complex crystallises in the triclinic space group P-1, with one dimeric complex and three CH$_3$CN molecules in the asymmetric unit (Fig. 3).  *N*-coordination (from the papaverine ligand) to Pd$^{II}$ leads to a pseudo-*anti* relationship of the two palladated ligands; the N(1)-Pd(1)-Pd(2)-N(2) torsion angle = 74.59(10)°; N(1)-Pd(1) and N(2)-Pd(s) bond distances = 2.033(2) Å and 2.032(2) Å, respectively.  The palladacyclic moiety 1 {containing Pd(1)} is found in a true boat conformation, with the Pd(1)-N(1)-C(9)-C(10) and Pd(1)-C(12)-C(11)-C(10) torsion angles < 2°.
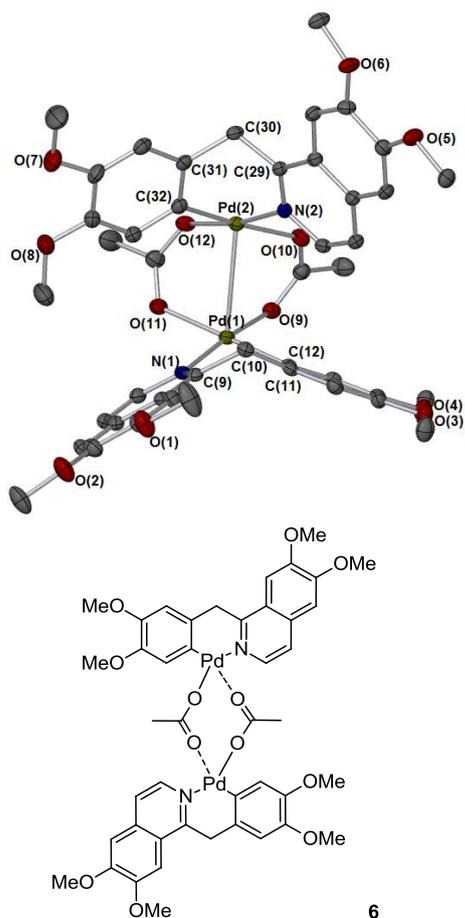
**Fig. 3** X-ray structure of **6** (a two-dimensional structure is included for clarity). 3 CH$_3$CN molecules and H-atoms omitted for clarity; selected atoms labelled. Thermal ellipsoids set at 50%.
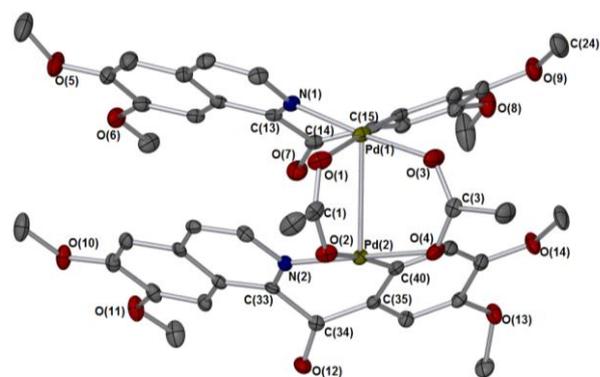


**Fig. 4** X-ray structure of **6'** (a two-dimensional structure is included for clarity). 2 (CH$_3$)$_2$SO molecules and H-atoms omitted for clarity; Thermal ellipsoids set at 50%.

Whereas the palladacyclic moiety 2 {containing Pd(2)} is slightly twisted as a result of modest π-π stacking interactions between neighbouring quinolinyl groups (*ca.* 4.1 Å between both aromatic ring systems). The Pd(2)-C(32)-C(31)-C(30) torsion angle of -6.1(3)° is the most pronounced. The Pd(1)-Pd(2) bond distance is 3.0258(4)Å. Thus in the solid-state and in the presence of CH$_3$CN, **5**·CH$_3$CN is not observed, and only binuclear Pd complex **6**·CH$_3$CN is obtained. Moreover, there was no sign of nitrite anion.

Of particular note is the finding that recrystallisation of **6** from DMSO gave isomer **6'** (not simply a DMSO adduct of **6**). This complex crystallised in the P2$_1$/c space group (*Z* = 4) and with several DMSO molecules in the unit cell. By contrast with **6**·CH$_3$CN, *N*-coordination to Pd$^{II}$ exhibits a pseudo-*syn* relationship and N(1)-Pd(1)-Pd(2)-N(2) torsion angle of -3.09(8)°. The two quinolinyl groups π-π stack intramolecularly, causing both palladacyclic moieties to form twisted boat conformations {*e.g.* Pd(1)-N(1)-C(13)-C(14) and Pd(1)-C(20)-C(15)-C(14) torsion angles of -14.2(3)° and 14.3(3)°, respectively}. Intermolecular π-π stacking is observed between neighbouring quinolinyl ring systems. The Pd(1)-Pd(2) bond distance is 2.9539(3) Å, and shorter than that found in **6**.
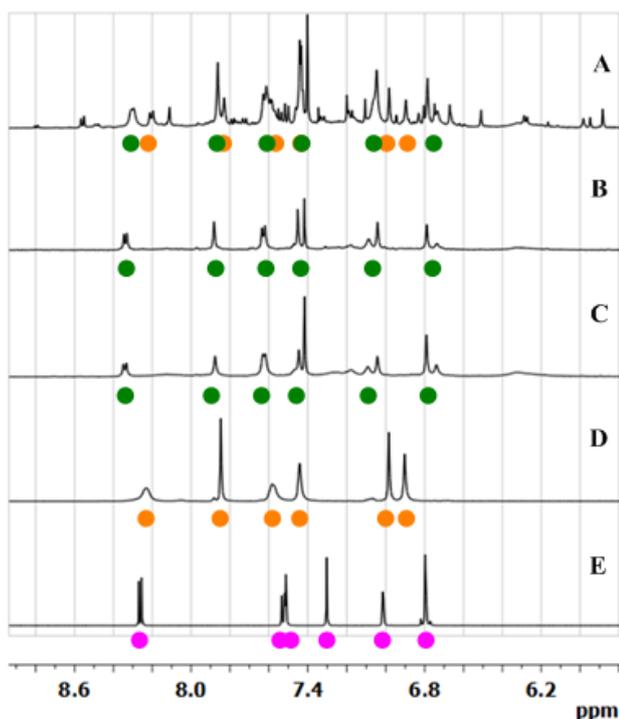
**Fig. 5** ^{1}H NMR spectra (400 MHz, in DMSO-$d_6$). **A**: Reaction of papaverine **3** with impure Pd(OAc)$_2$ (orange circles indicate complex **4**, green circles complex **6** (mixture of isomers/mononuclear-dinuclear species), and magenta circles **3**). **B**: Reaction of papaverine with pure Pd(OAc)$_2$. **C**: Crystals of **6**. **D**: Pd(NO$_2$)(C^N)CH$_3$CN·1.5H$_2$O (denoted as **4**·CH$_3$CN). **E**: papaverine (**3**) (note: the signal at δ6.8 integrates for 2H, thus 7H in total in the aromatic region).
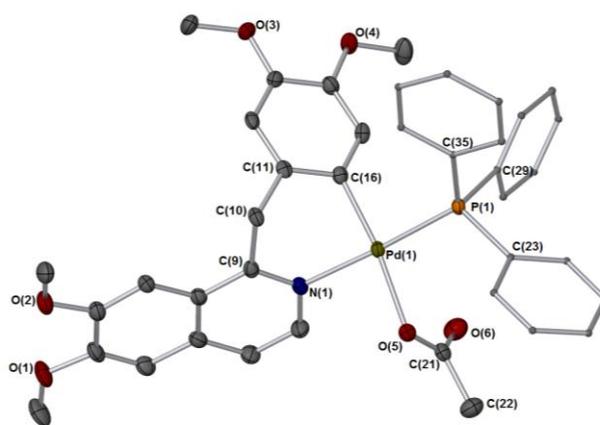
The reaction of an impure batch of Pd(OAc)$_2$ (*ca.* 81% Pd$_3$(OAc)$_5$NO$_2$) with papaverine **3**, in dry CH$_3$CN and under a N$_2$ atmosphere, afforded a mixture of products (Fig. 5, spectrum **A**). A similar spectrum was observed on running the reaction (not shown) in the presence of air (note: papaverine **3**, indicated by magenta circles, does not precipitate from CH$_3$CN solutions; also, **3** is not observed in the crude ^{1}H NMR spectra of the reaction products). The equivalent reaction run with pure Pd(OAc)$_2$ (>99%) afforded what appears to be a cyclometallated product in 64% yield (green circles), which has the same ^{1}H NMR spectrum as the crystalline material of **6** (compare spectra **B** and **C**, Fig. 5). This material is either a mixture of isomeric dinuclear compounds in DMSO-$d_6$ solution, or mononuclear and dinuclear compounds. Dissolution of crystalline **6** in pyridine-$d_5$ gave a single mononuclear complex [Pd(OAc)(C^N)pyr-$d_5$], (**5**·pyr-$d_5$) (see E.S.I.). Moreover, a stable phosphine adduct of **6** could be formed by reaction with PPh$_3$ (1:1, Pd$^{II}$:PPh$_3$) affording mononuclear complex [Pd(OAc)(C^N)PPh$_3$] (**7**) in 78% yield. ^{1}H NMR spectroscopy showed the expected four singlet proton resonances for the methoxy groups at δ 4.09, 3.97, 3.69 and 2.91; proton resonances for papaverine and phenyl moieties, two pseudo-diastereotopic palladacylic methylene protons (δ 4.96 4.82, broad doublets, $^2J_{H,H}$ *ca.* 12 Hz), and methyl singlet resonance for the acetoxy group (δ 1.21). An X-ray structure showed that complex **7** crystallised in the monoclimic $C2/c$ space group (Fig. 6).



**Fig. 6** X-ray structure of [Pd(OAc)(C^N)PPh$_3$] (**7**). 1 CH$_2$Cl$_2$ and H-atoms omitted for clarity; Thermal ellipsoids set at 50% (with the exception of the phenyl groups at P).

The N(1)-Pd(1) bond distance {2.091(2) Å} is longer than the equivalent N-Pd bonds found in both **6** and **6'** (*ca.* 2.009-2.033 Å). The palladacycle once again sits in a boat conformation. The ratio of OAc:NO$_2$ containing-products in spectrum **A** is estimated as 1:0.6 (by ^{1}H NMR spectroscopy), and whilst this does not match the OAc:NO$_2$ ratio in the impure Pd(OAc)$_2$ batch, it can be accounted for by the low overall yield (27%) (which is consistent with considerable Pd$^{II}$ degradation and Pd$^0$ black formation).

To account for the other major component in spectrum **A** (Fig. 6) an authenitic sample of **4** needed to be prepared. Reaction of **6**·CH$_3$CN with NaNO$_2$ (10 eq.) gave **4** in 66% yield (exact composition [Pd(NO$_2$)(C^N)CH$_3$CN]1.5H$_2$O, which compares well to the reported composition [Pd(NO$_2$)(C^N)CH$_3$CN]3H$_2$O; the ^{1}H NMR spectrum (in DMSO-$d_6$) is shown as **D** (Fig. 6),[15a,19] which resembles the other component in the reaction of **3** with impure Pd(OAc)$_2$ (orange circles). Thus, using impure Pd(OAc)$_2$ both CH$_3$CN adducts of **4** and **6** are observed under the reaction conditions, whereas using pure Pd(OAc)$_2$, **6** is the only product (as a mixture isomeric, mononuclear or dinuclear compounds, verified by the independent synthesis of **7**). We therefore conclude that nitrite impurities explain the formation of nitrite adducts from Pd(OAc)$_2$ and papaverine **3** (in the presence or absence of air).

**Photocrystallography.**

In preparing the authentic sample of complex **4** we were keen to crystallographically characterise its structure. Whilst this was not possible for either **4**·CH$_3$CN or **4**·DMSO,[15c] we were able to prepare the PPh$_3$ adduct from the reaction of **4**·CH$_3$CN with PPh$_3$ (1:1 ratio) in CH$_2$Cl$_2$ at reflux for 2 h. ^{1}H and ^{31}P NMR spectroscopy showed the presence of only one compound, proposed as being [Pd(NO$_2$)(C^N)PPh$_3$] **8** (formed quantitatively). A single crystal of this complex was initially studied by X-ray diffraction methods (in York), revealing that the PPh$_3$ was coordinated (as expected), but as a mixture 'Pd-η$^1$-*N*O$_2$' (**8a**) and 'Pd-η$^1$-*O*NO' (**8b**) isomers. It is known that nitrito complexes of Ni$^{II}$ exhibit linkage isomerisation (by photoexcitation), indeed examples are of interest as potential data storage devices.[20] Thus, more comprehensive

photocrystallographic experiments were conducted using synchrotron radiation.

An X-ray data set was collected in the absence of light at 150 K on beamline I19 at the Diamond Light Source, Rutherford Appleton Laboratory, UK, and the structure solved and refined. The complex **8** crystallizes in the monoclinic space group $P2_1/c$ and exists as a *ca.* 1:3 mixture of 'Pd-$\eta^1$-$NO_2$' (**8a**) and 'Pd-$\eta^1$-$O$NO' (**8b**) linkage isomers (Table 1 and Fig. 7) at this temperature. The crystal was then irradiated at 150 K using a specifically designed LED ring,[21] which supports six 400 nm LEDs in a circle, 1 cm from the crystal to ensure uniform irradiation. After 1 h the crystal structure was redetermined and it was found that the photoactivated nitrito complex 'Pd-$\eta^1$-$O$NO' (**8b**) is fully formed (100% conversion). Further irradiation (1.5 h) caused no appreciable change, confirming the 100% nitrito form to be a photostationary state. Notably, this isomer is retained at 150 K in the dark (over 1 h), showing that the system is metastable under these conditions. The Pd-$\eta^1$-$O$NO' (**8b**) isomeric structure remains in the same space group $P2_1/c$, with little change in the packing arrangement and only a $\Delta V = 0.14\%$ increase in the unit cell volume observed, in comparison to the initially determined mixed-isomer structure. Variable temperature parametric studies (VT) determined that the metastable state exists on warming to 180 K, however further heating to 200 K causes the system to revert back to its mixed-isomer structure initially observed at 150 K.

Recent studies for another mixed nitro:nitrito Ni[II] complex have shown that conversion between isomers can also be controlled thermally.[22] As such, in separate experiments on Station 11.3.1 at the Advanced Light Source, Berkeley, California, USA, a single crystal of **8** was slow-cooled *in-situ* and a series of identical datasets collected at regular intervals to monitor any changes in nitro:nitrito occupation. Conversion to the nitrito isomer, **8b**, was found to increase, from 76% at ambient temperature to a maximum 86% on slow-cooling to 150 K (Table 2).

**Table 1** Crystallographically determined percentage ratios of **8a** and **8b** in a single crystal as a function of exposure to 400 nm radiation and variable temperature.

| Experiment | Irradiation time / h | Temp / K | Conversion / % | |
|---|---|---|---|---|
| | | | **8a** | **8b** |
| GS[a] | 0 | 150 | 23 | 77 |
| UV | 1 | 150 | 0 | 100 |
| UV | 1.5 | 150 | 0 | 100[b] |
| 1 h Dark | 1.5 | 150 | 0 | 100[c] |
| VT[d] | 1.5 | 160 | 0 | 100 |
| VT[d] | 1.5 | 180 | 0 | 100 |
| VT[d] | 1.5 | 200 | 23 | 77 |

[a] GS = ground state. [b] Photostationary state. [c] System is metastable at 150 K (**8b**). [d] VT = variable temperature.

**Table 2** Crystallographically determined percentage of **8b** in a single crystal as a function of temperature.

| Temp / K | **8b** / % |
|---|---|
| 298 | 76 |
| 250 | 78 |
| 200 | 84 |
| 150 | 86 |

The increase in **8b** on slowly decreasing the temperature indicates that the major component is the more thermodynamically stable isomer at lower temperatures, which correlates with results obtained for the Ni[II] system.[22] The close agreement between the conversion observed at room temperature and the initial structure determined in the photocrystallographic experiments indicate that flash-cooling of the crystal appears to thermally trap the system in its ambient state.
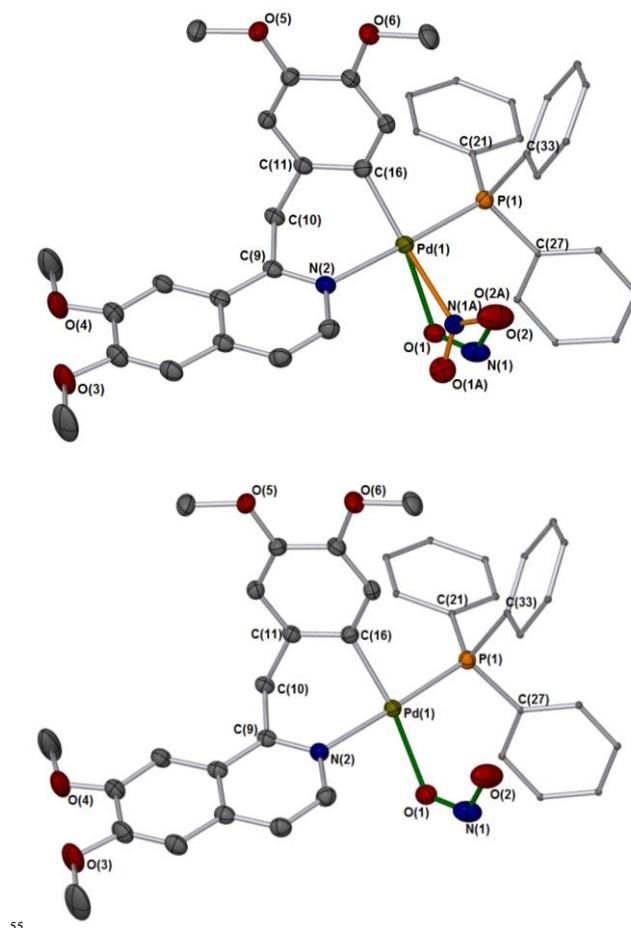


**Fig. 7** X-ray diffraction analysis of complex **8** (the thermal ellipsoids are set at 50%, with the exception of the phenyl groups at P). Top: Ground state structure (150 K) showing a mixture of 'Pd-$\eta^1$-$NO_2$' (**8a**) and 'Pd-$\eta^1$-$O$NO' (**8b**) isomers. Bottom: Following UV irradiation for 1 h.

In summary, the appearance of nitrite anion in Pd(OAc)(NO_2)(pip)_2 can be traced to nitrite impurities found in some commercial sources of Pd(OAc)_2. Furthermore, the appearance of nitrite anion in a palladacycle-derived from papaverine **3** and Pd(OAc)_2 in CH_3CN can be explained in the

same way. The impact of nitrite impurities in two catalytic reactions[13,14] has been assessed; $Pd_3(OAc)_6$ and $Pd_3(OAc)_5NO_2$ exhibiting similar catalytic efficacy. Reductive elimination of nitrite and organic fragments from $Pd^{II}/Pd^{IV}$, leading to C-NO_2 bond formation, is slow[23] thus $NO_2^-$ can be considered as a spectator ligand. Our studies highlight the need to assess the effect of nitrite impurities in reactions involving $Pd(OAc)_2$, especially in stoichiometric coordination chemistry. We have determined that $NO_2^-$ is not generated *in situ* in the reactions detailed above. The interesting solid-state isomerism behaviour in the palladacyclic complex **8** marks the first reported observation of nitro-nitrito linkage isomerism in a $Pd^{II}$ complex, with both the photocrystallographic and thermal investigations comparing well with other studies involving nitro-nitrito linkage isomers.[20,21] This type of linkage isomerisation could be important in the transfer of nitrite to organic fragments, *e.g.* in C-N bonding forming processes. Reductive elimination of nitrite, leading to C-N bond-formation (*e.g.* nitration of papaverine) has not been observed in our study, an outcome that can be explained by the 'Pd-ONO' form being the predominant isomer in these palladacycles (C-O bond formation is considered unlikely). Crucially, this part of our study demonstrates the uniqueness of the catalytic 'C-NO_2' bond forming process that has recently been developed by Buchwald and co-workers.[23a] Accordingly, it would be interesting to study reductive elimination from 'Pd-NO_2'/'Pd-ONO' species.

## Notes and references

*[a] Department of Chemistry, University of York, York, YO10 5DD, UK. Fax: 0044 (0)1904 322516; Tel: 0044 324091; E-mail: ian.fairlamb@york.ac.uk*
*[b] Department of Biology, University of York, York, YO10 5DD, UK. Tel: 0044 (0)1904 328828.*
*[c] Department of Chemistry, University of Bath, Bath, BA2 7AY, UK. Fax: 0044 (0)1225 383 183; E-mail: p.r.raithby@bath.ac.uk*
*[d] Diamond Light Source Ltd, Diamond House, Harwell Science and Innovation Campus, Didcot, Oxfordshire OX11 0DE.*
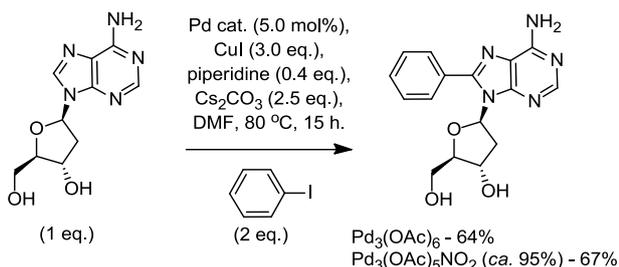*[e] Advanced Light Source, Lawrence Berkeley National Laboratory Berkeley, Berkeley, CA 94720-8229, USA.*

† Electronic Supplementary Information (ESI) available: [Synthetic procedures, characterisation data and details of X-ray crystallographic experiments]. See DOI: 10.1039/b000000x/
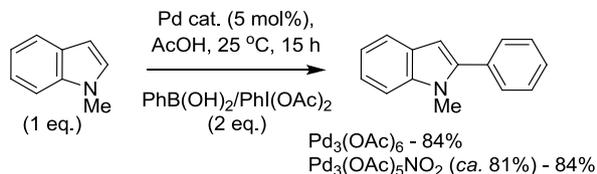
1   In recent times, several commercial suppliers have been offering high purity "$Pd(OAc)_2$" which shows superior reactivity in some chemical processes. For example, low yields have been reported for some $Pd^{II}$ complexes derived from $Pd(OAc)_2$, see: C. E. Anderson, S. F. Kirsch, L. E. Overman, C. J. Richards, and M. P. Watson, *Organic Syntheses*, 2007, **84**, 148; *Coll. Vol.* 11, 2009, 714; (b) "Palladium(II) Acetate, Recrystallized" in *Aldrichimica Acta* 2010, **43**, 1; (c) See supporting information in: A. J. Young, and M. C. White, *J. Am. Chem. Soc.*, 2008, **130**, 14090. It is not clear whether nitrite impurities are responsible for the difficulties encountered in these studies. For precautions concerning the use of $Pd(OAc)_2$ in the synthesis of $Pd(OAc)_2(dppe)$, see: C. Bianchini, A. Meli, and W. Oberhauser, *Organometallics*, 2003, **22**, 4281.

2   Given the large number of research papers published using palladium(II) acetate, and limited reports reporting any serious problems between batches and suppliers, we presume that the quality of the material has not been an issue for the vast majority of applications. A search of ISI Web of Knowledge revealed 2815 hits for "palladium acetate" and 1113 hits for palladium(II) acetate.

3   For general halide effects, see: (a) S. Verbeeck, C. Meyers, P. Franck, A. Jutand, and B. U. W. Maes, *Chem. Eur. J.*, 2010, **16**, 12831, and references therein. For effects on succinimide anions, see: (b) C. M. Crawforth, I. J. S. Fairlamb, A. R. Kapdi, J. L. Serrano, R. J. K. Taylor, and G. Sanchez, *Adv. Synth. Catal.*, 2006, **348**, 405. (c) I. J. S. Fairlamb, R. J. K. Taylor, J. L. Serrano, and G. Sanchez, *New J. Chem.*, 2006, **30**, 1695. (d) S. Burling, C. M. Crawforth, I. J. S. Fairlamb, A. R. Kapdi, R. J. K. Taylor, and A. C. Whitwood, *Tetrahedron*, 2005, **61**, 9736. (e) C. M. Crawforth, S. Burling, I. J. S. Fairlamb, R. J. K. Taylor, A. C. Whitwood, *Chem Commun.*, 2003, 2194. For papers detailing *N*-halosuccinimide as a substrate (at $Pd^{IV}$), see: (f) S. R. Whitfield, and M. S. Sanford, *J. Am. Chem. Soc.*, 2007, **129**, 15142. For N-imidate ligand effects in $Au^{III}$ catalysis, see: (g) J. P. Reeds, A. C. Whitwood, M. P. Healy, and I. J. S. Fairlamb, *Chem. Commun.*, 2010, **46**, 2046.

4   (a) T. E. Storr, A. G. Firth, K. Wilson, K. Darley, C. G. Baumann, and I. J. S. Fairlamb, *Tetrahedron*, 2008, **64**, 6125; (b) T. E. Storr, C. G. Baumann, R. J. Thatcher, S. De Ornellas, A. C. Whitwood, and I. J. S. Fairlamb, *J. Org. Chem.*, 2009, **74**, 5810; (c) T. E. Storr, J. A. Strohmeier, C. G. Baumann, and I. J. S. Fairlamb, *Chem. Commun.*, 2010, **46**, 6470.

5   B. Tao, and D. W. Boykin, *J. Org. Chem.*, 2004, **69**, 4330.

6   Previously we have determined the X-ray structure of the bis-hydrate of $Pd(OAc)_2(pip)_2$, see ref. 4b.

7   This $Pd-NO_2$ bond distance is very similar to other reported '$Pd-NO_2$' complexes (see ref. 15b).

8   Considered were the: i) oxidation of piperidine; ii) intramolecular acetate (nucleophilic) attack on a $Pd^{II}$ coordinated acetonitrile ligand; iii) reduction of nitrate to nitrite by Pd/H_2, see: (a) S. Hörold, K. D. Vorlop, T. Tacke, and M. Sell, *Catal. Today*, 1993, **17**, 21. (b) K. A. Guy, H. Xu, J. C. Yang, C. J. Werth, and J. R. Shapley, *J. Phys. Chem. C*, 2009, **113**, 8177.

9   (a) V. I. Bakhmutov, J. F. Berry, F. A. Cotton, S. Ibragimov, and C. A. Murillo, *Dalton Trans.*, 2005, 1989. For details on the speciation of "$Pd(OAc)_2$" under various conditions, see: (b) L. A. Adrio, B. N. Nguyen, G. Guilera, A. G. Livingston, and K. K. Hii, *Catal. Sci. Technol.*, 2011, DOI: 10.1039/c1cy00241d.

10  The fully balanced equation is: $3Pd^0+6HNO_3+6HOAc \rightarrow Pd_3(OAc)_6+6NO_2+6H_2O$.

11  $Pd_3(OAc)_5NO_2$ can only be isolated by manual picking of the crystals from $Pd_3(OAc)_6$ (see ref. 9a).

12  Caution should be exercised in using elemental analysis to determine the amount of $Pd_3(OAc)_5NO_2$ at low levels (<10%). $^1$H NMR spectroscopic analysis shows this impurity at >2% levels.

13  The direct arylation of 2'-deoxyadenosine mediated by a Pd/Cu system was tested as this had been sensitive Pd catalyst source in the past (see ref. 4b). $Pd_3(OAc)_6$ (>99%) and $Pd_3(OAc)_5NO_2$ (*ca.* 95%) equally facilitate the reaction within experimental error.

Pd cat. (5.0 mol%),
CuI (3.0 eq.),
piperidine (0.4 eq.),
Cs$_2$CO$_3$ (2.5 eq.),
DMF, 80 °C, 15 h.

(1 eq.)   (2 eq.)

Pd$_3$(OAc)$_6$ - 64%
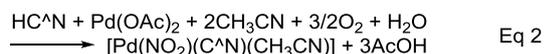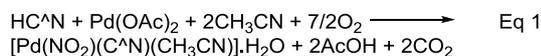Pd$_3$(OAc)$_5$NO$_2$ (*ca.* 95%) - 67%

14 The C2-arylation of indole, involving Pd$^{II}$/Pd$^{IV}$ catalytic cycles, was also evaluated. No difference in the product yields, using either Pd$_3$(OAc)$_6$ (>99%) or Pd(OAc)$_5$NO$_2$ (*ca.* 81%) was recorded:

Pd cat. (5 mol%),
AcOH, 25 °C, 15 h

(1 eq.)

PhB(OH)$_2$/PhI(OAc)$_2$
(2 eq.)

Pd$_3$(OAc)$_6$ - 84%
Pd$_3$(OAc)$_5$NO$_2$ (*ca.* 81%) - 84%

For further details, see: N. R. Deprez, D. Kalyani, A. Krause, and M. S. Sanford, *J. Am. Chem. Soc.*, 2006, **128**, 4972.

15 (a) M. Nonoyama, *Synth. React. Inorg. Met.-Org. Chem.*, 1999, **29**, 119. (b) M. Nonoyama, and K. Nakajima, *Polyhedron*, 1999, **18**, 533. (c) X-ray structures containing a C^N palladacycle have been determined in ref. 15b. However, there are no reported X-ray structures of papaverine-derived Pd-complexes.

16 Two balanced chemical equations (1 and 2, below) were proposed (refs. 15a,b) to account for the original observations (note that metallic Pd is not included in these chemical equations):

HC^N + Pd(OAc)$_2$ + 2CH$_3$CN + 7/2O$_2$ $\longrightarrow$ Eq 1
[Pd(NO$_2$)(C^N)(CH$_3$CN)]**·**H$_2$O + 2AcOH + 2CO$_2$

HC^N + Pd(OAc)$_2$ + 2CH$_3$CN + 3/2O$_2$ + H$_2$O
$\longrightarrow$ [Pd(NO$_2$)(C^N)(CH$_3$CN)] + 3AcOH     Eq 2

The principles governing formation of nitrogen oxides from the oxidation of acetonitrile on copper-chromium and platinum catalysts (typically > 300 °C) are known, see: T. L. Susharina, M. A. Kerzhentsev, O. Y. Pod'yacheva, and Z. R. I smagilov, *React. Kinet. Catal. Lett.*, 1986, **31**, 27-33.

17 In all of the reactions carried out the formation of Pd black (non-characterised) was noted.

18 In the original paper (ref. 15a), crystalline material precipitated within a day.

19 The independent synthesis of [Pd(NO$_2$)(C^N)CH$_3$CN] has been conducted under various conditions (*e.g.* under N$_2$ or air, with dry and reagent grade solvent, 5 or 10 eq. of NaNO$_2$, or the use of KNO$_2$). The precise composition of **4**·xCH$_3$CN·yH$_2$O varies according to the conditions used. In several cases, elemental analysis has indicated that a small quantity of MNO$_2$ (M = Na or K) remains in the product. In one example, a single crystal of a new complex was formed, which is Pd(NO$_2$)$_2$(*N*-Hpap)$_2$, where the papaverine is coordinated through the pyridyl nitrogen atom only. The single crystal X-ray structure of this complex, and an explanation for its formation, is shown in the ESI.

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21 S. K. Brayshaw, J. W. Knight, P. R. Raithby, T. L. Savarese, S. Schiffers, S. J. Teat, J. E. Warren, and M. R. Warren, *J. App. Cryst.*, 2010, **43**, 337.

22 L. E. Hatcher, M. R. Warren, D. R. Allan, S. K. Brayshaw, A. L. Johnson, S. Fuertes, S. Schiffers, A. J. Stevenson, S. J. Teat, C. H. Woodall, and P. R. Raithby, *Angew. Chem.*, *Int. Ed.*, 2011, **50**, 8371.

23 With Pd$^0$/Pd$^{II}$ catalytic cycles, using $^t$BuBrettPhos, reductive elimination leading to C-NO$_2$ bond formation, has been reported, see: (a) B. P. Fors, and S. L. Buchwald, *J. Am. Chem. Soc.*, 2009, **131**, 12898. To the best of our knowledge reductive elimination from Pd$^{IV}$ leading to C-NO$_2$ bond formation has not been reported, though a C-CF$_3$ bond-forming reaction at Pd$^{IV}$ has been recently noted, see: (b) N. D. Ball, J. B. Gary, Y. Ye, and M. S. Sanford, *J. Am. Chem. Soc.*, 2011, **133**, 7577.