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# Iodonium Salts Are Key Intermediates in Pd-Catalyzed Acetoxylation of Pyrroles

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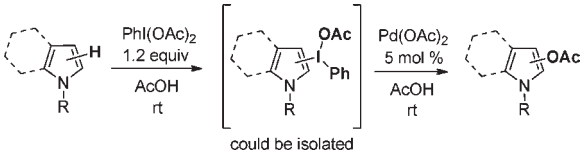
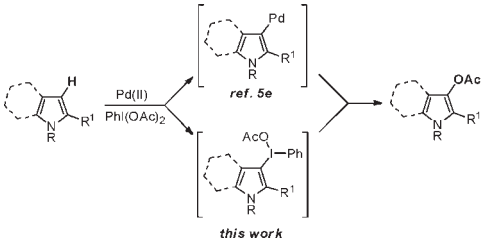
## ABSTRACT




**A mild, room-temperature Pd-catalyzed acetoxylation of pyrroles with phenyliodonium acetate is described. The acetoxylation was found to proceed via the initial formation of pyrrolyl(phenyl)iodonium acetates, which were converted to acetoxypyrroles in the presence of $Pd(OAc)_2$. The acetoxylation could also be carried out as a one-pot sequential procedure without the isolation of the intermediate iodonium salts.**

Transition metal catalyzed selective C−H oxidation is an efficient methodology for the construction of C−O bonds.[1] The regioselectivity of the C−H activation/oxidation in aromatic systems usually is controlled by suitable *ortho*-directing groups.[2] Intriguingly, in contrast to the many examples of C−O bond formation in benzene rings,[3] the direct acetoxylation of heterocycles is much less explored.[4] Thus, there are only a few reports on direct acetoxylation of heterocycles, and the scope of substrates is limited to indoles[5] and uracil.[6] It should be noted that the regioselectivity of C−O bond formation in heterocycles typically is controlled by the inherent reactivity of a given heterocyclic system and, consequently, there is no need for the *ortho*-directing group.

Direct acetoxylation examples frequently employ $Pd(OAc)_2$ as a catalyst and $PhI(OAc)_2$ as a terminal oxidant in acetic acid, conditions that have been developed by Crabtree.[7] Mechanistic studies evidence that the Pd-catalyzed direct acetoxylation involves palladation of an aryl C−H bond with Pd(II) species as the first step,[8] which is followed by oxidation to dinuclear Pd(III) complexes[9] and, finally, product forming reductive elimination. By analogy, carbopalladation via C−H activation was considered to be the initial step also in Pd-catalyzed acetoxylation of indoles (eq 1).[5e]




(1)

The present report on a selective oxidation of substituted pyrroles[10] expands the scope of heterocycles for the

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(2) (a) Lyons, T. W.; Sanford, M. S. *Chem. Rev.* **2010**, *110*, 1147. (b) Daugulis, O.; Zaitsev, V. G.; Shabashov, D.; Pham, Q.-N.; Lazareva, A. *Synlett* **2006**, 3382. (c) Yu, J.-Q.; Giri, R.; Chen, X. *Org. Biomol. Chem.* **2006**, *4*, 4041.

(3) Selected recent examples of Pd-catalyzed C−H activation/oxidation of arenes: (a) Richter, H.; Beckendorf, S.; Mancheno, O. G. *Adv. Synth. Catal.* **2011**, *353*, 295. (b) Chernyak, N.; Dudnik, A. S.; Huang, C.; Gevorgyan, V. *J. Am. Chem. Soc.* **2010**, *132*, 8270. (c) Neufeldt, S. R.; Sanford, M. S. *Org. Lett.* **2010**, *12*, 532. (d) Zheng, X.; Song, B.; Xu, B. *Eur. J. Org. Chem.* **2010**, *23*, 4376. (e) Vickers, C. J.; Mei, T.-S.; Yu, J.-Q. *Org. Lett.* **2010**, *12*, 2511. (f) Wang, X.; Lu, Y.; Dai, H.-D; Yu, J.-Q. *J. Am. Chem. Soc.* **2010**, *132*, 12203. (g) Wang, G.-W.; Yuan, T.-T. *J. Org. Chem.* **2010**, *75*, 476. (h) Zhang, Y.-H.; Yu, J.-Q. *J. Am. Chem. Soc.* **2009**, *131*, 14654.

(4) For reviews on C−H activation/functionalization of heterocycles, see: (a) Beck, E. M.; Gaunt, M. J. *Top. Curr. Chem.* **2010**, *292*, 85. (b) Ackermann, L.; Vicente, R.; Kapdi, A. R. *Angew. Chem., Int. Ed.* **2009**, *48*, 9792. (c) Xiao, C.; Engle, K. M.; Wang, D.-H.; Yu, J.-Q. *Angew. Chem., Int. Ed.* **2009**, *48*, 5094. (d) Seregin, I. V.; Gevorgyan, V. *Chem. Soc. Rev.* **2007**, *36*, 1173. (e) Bellina, F.; Rossi, R. *Tetrahedron* **2009**, *65*, 10269.

(5) (a) Choy, P. Y.; Lau, C. P.; Kwong, F. Y. *J. Org. Chem.* **2011**, *76*, 80. (b) Liu, Q.; Li, G.; Yi, H.; Wu, P.; Liu, J.; Lei, A. *Chem.—Eur. J.* **2011**, *17*, 2353. (c) Liang, Z.; Zhao, J.; Zhang, Y. *J. Org. Chem.* **2010**, *75*, 170. (d) Liu, K.; Wen, P.; Liu, J.; Huang, G. *Synthesis* **2010**, 3623. (e) Mutule, I.; Suna, E.; Olofsson, K.; Pelcman, B. *J. Org. Chem.* **2009**, *74*, 7195.

(6) Lee, H. S.; Kim, S. H.; Kim, J. N. *Bull. Korean Chem. Soc.* **2010**, *31*, 238.

(7) Yoneyama, T.; Crabtree, R. H. *J. Mol. Catal. A* **1996**, *108*, 35.

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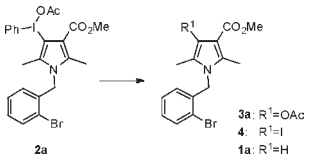
Pd-catalyzed acetoxylation reaction. Also, we provide evidence that the acetoxylation of electron-rich heterocycles such as pyrroles and indoles under Crabtree conditions most likely occurs via the initial formation of heteroaryliodonium acetates (eq 1).[11] The latter are transformed into an acetoxylated product in the presence of a Pd catalyst.

Initially, Crabtree acetoxylation conditions were examined for synthesis of acetoxypyrroles and the progress of the reaction was followed by NMR methods. Thus, stirring the pyrrole **1a** with $Pd(OAc)_2$ (5 mol %) and $PhI(OAc)_2$ (2 equiv) in AcOH-$d_4$ showed complete conversion within 2 h at ambient temperature.[12] Two sets of signals in a 3.5:1 ratio were observed in the $^1H$ NMR spectrum of the reaction mixture. The minor set of signals corresponded to acetoxypyrrole **3a**, whereas the major set of signals was assigned to a structure of pyrrolyliodonium acetate **2a** based on $^1H$ NMR, $^{13}C$ NMR, MS data and X-ray crystallographic analysis of purified **2a**.

The iodonium acetate **2a** was stable in AcOH-$d_4$ solution at rt (entry 1, Table 1). However, in the presence of 5 mol % $Pd(OAc)_2$ in AcOH-$d_4$, **2a** was converted into the target acetoxypyrrole **3a** (90% yield) within 18 h (entry 2). Acetonitrile was equally efficient to AcOH, affording **3a** in 91% yield (entry 3). Additional experiments were performed to investigate the reactivity of iodonium salt **2a**. Heating of **2a** without the Pd catalyst yielded a mixture of products **3a**, **4**, and the starting **1a** (entry 4). Interestingly, only unreacted **2a** was observed after prolonged heating in $(CF_3)_2CHOH$, a solvent of choice for oxidative nucleophilic acetoxylation of alkylphenyl ethers (entry 5).[13] $PtCl_2$ was inferior to $Pd(OAc)_2$ as a catalyst[5e] (entry 6), whereas $PtCl_4$ did not catalyze the conversion of **2a** (entry 7). Likewise, $BF_3{\bullet}OEt_2$[14] in DCM (entry 8) and $Cu(OTf)_2$ in DCM[15] were not efficient as catalysts (entries 8, 9), whereas addition of TMS-OTf[16] resulted in the formation of an inseparable mixture of products (entry 10).

**Table 1.** Reactivity of Arylpyrrolyliodonium Acetate **2a**




| entry | catalyst (mol %) | solvent | $t$ (°C) | time (h) | products (yield, %) |
|---|---|---|---|---|---|
| 1 | – | AcOH | rt | 18 | **2a** |
| 2 | $Pd(OAc)_2$ (5) | AcOH | rt | 18 | **3a** (90%) |
| 3 | $Pd(OAc)_2$ (5) | MeCN | 60 | 18 | **3a** (91%) |
| 4 | – | AcOH | 100 | 24 | **3a** (45%) + **4** (20%) + **1a** (27%) |
| 5 | – | HFIP | 100 | 18 | **2a** |
| 6 | $PtCl_2$ (5) | AcOH | 80 | 48 | **3a**:**1a** = 3:2 |
| 7 | $PtCl_4$ (5) | AcOH | 80 | 48 | **2a** |
| 8 | $BF_3{\bullet}OEt_2$ (400) | $CH_2Cl_2$ | rt | 3 | **2a** |
| 9 | $Cu(OTf)_2$ (10) | $CH_2Cl_2$ | 35 | 24 | **2a** |
| 10 | TMS-OTf (200) | HFIP | rt | 2 | products mixture |

A series of pyrrolyliodonium acetates **2b**–**k** was subsequently prepared in the reaction of pyrroles **1b**–**k** with 1.2 equiv of $PhI(OAc)_2$ in AcOH at ambient temperature (63–79% yields; see Table 2). The iodonium acetates **2b**–**k** were sufficiently stable to be isolated and characterized,[17] and they can be stored in the freezer for several months. To the best of our knowledge, pyrrolyl-3-iodonium acetates have not been previously prepared in a direct electrophilic substitution of pyrrole.[18]

The yields of iodonium salts **2a**–**k** were found to be sensitive to the electronic properties of substituents on the pyrrole ring.[19] Iodonium acetates were formed from *N*-unsubstituted pyrroles **2h,k** (entries 8,11, Table 2). The regioselectivity of pyrrolyliodonium salt formation apparently is a result of the combined directing effects of pyrrole substituents.[20] Nevertheless, there is a strong preference for the formation of iodonium salts at the α-position (entries 2, 3, 9, 10),[21] and $\beta$-pyrrolyliodonium salts could be obtained only for 2,5-disubstuted heterocycles **1a,e**–**h,k** (entries 1, 5–8, 11, Table 2).

In the presence of 5 mol % $Pd(OAc)_2$ in AcOH solution at ambient temperature iodonium salts **2a**–**k**

(8) It has been shown that cyclopalladation is the rate-limiting step of the acetoxylation reaction: Stowers, K. J.; Sanford, M. S. *Org. Lett.* **2009**, *11*, 4584.

(9) (a) Powers, D.; Ritter, T. *Top. Organomet. Chem.* **2011**, *35*, 129. (b) Powers, D. C.; Ritter, T. *Nat. Chem.* **2009**, *1*, 302.

(10) (a) The 3-hydroxypyrrole subunit is incorporated into Obatoclax, an experimental drug candidate for the treatment of various types of cancer: *Drugs Future*, **2007**, *32*, 228. Substituted 3-hydroxypyrroles have also been employed: (b) as anti-tumor agents: Cholody, W. M.; Petukhova, V.; O'Brien, S.; Ohler, N.; Pikul, S. WO 011675 *A1*, 2005; *Chem. Abstr.* **2005**, *142*, 197868. (c) in the design of DNA-binding ligands: Wellenzohn, B.; Loferer, M. J.; Trieb, M.; Rauch, C.; Winger, R. H.; Mayer, E.; Liedl, K. R. *J. Am. Chem. Soc.* **2003**, *125*, 1088.

(11) Consequently, the acetoxylation with $PhI(OAc)_2$ does not involve a C–H activation step by a Pd catalyst. The role of transition metal catalysts has recently been reinvestigated also in other $PhI(OAc)_2$ mediated reactions; see: (a) Kang, Y.-B.; Gade, L. H. *J. Am. Chem. Soc.* **2011**, *133*, 3658. (b) Cho, S. H.; Yoon, J.; Chang, S. *J. Am. Chem. Soc.* **2011**, *133*, 5996.

(12) The use of $Pd(OAc)_2$ together with other oxidants such as $PhCO_3tBu$ (2 equiv, 65 °C, $Ac_2O$, 21 h), *m*-CPBA (2 equiv, 100 °C, AcOH, 2 h), $K_2S_2O_8$ (2 equiv, 100 °C, AcOH, 2 h), and Oxone (2 equiv, 100 °C, AcOH, 2 h) did not afford the acetoxylated pyrrole **3a**.

(13) Kita, Y.; Tohma, H.; Hatanaka, K.; Takada, T.; Fujita, S.; Mitoh, S.; Sakurai, H.; Oka, S. *J. Am. Chem. Soc.* **1994**, *116*, 3684.

(14) Dohi, T.; Morimoto, K.; Takenaga, N.; Goto, A.; Maruyama, A.; Kiyono, Y.; Tohma, H.; Kita, Y. *J. Org. Chem.* **2007**, *72*, 109.

(15) Phipps, R. J.; Grimster, N. P.; Gaunt, M. J. *J. Am. Chem. Soc.* **2008**, *130*, 8172.

(16) Dohi, T.; Ito, M.; Yamaoka, N.; Morimoto., K.; Fujioka, H.; Kita, Y. *Angew. Chem., Int. Ed.* **2010**, *49*, 3334.

(17) The majority of solid aryliodonium acetates **2b**–**k** are hygroscopic and decompose at temperatures above 25 °C. However, they are stable in acetic acid solutions.

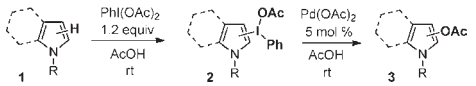
(18) Single report on preparation of pyrrolyl-3-iodonium triflates from 3-trimethylsilylpyrrole: Liu, J.-H.; Chan, H.-W.; Xue, F.; Wang, Q.-G.; Mak, T. C. W.; Wong, H. N. C. *J. Org. Chem.* **1999**, *64*, 1630.

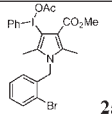
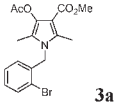
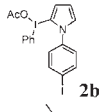
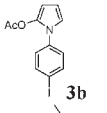
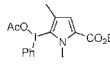
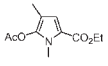
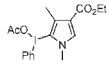
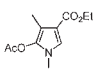
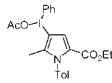
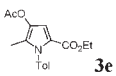
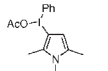
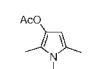
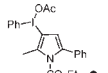
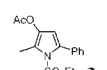
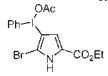
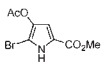
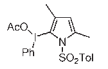
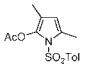
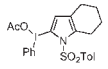
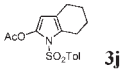
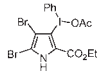
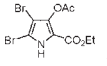
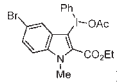
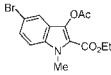
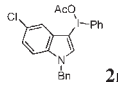
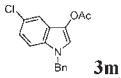
(19) Correlation between yields of phenyliodonium salts and Hammett $\sigma$ constants of substituents has been reported: Dohi, T.; Yamaoka, N.; Kita, Y. *Tetrahedron* **2010**, *66*, 5775. See also the Supporting Information, p S26.

(20) For substituent effect on regioselectivity of $S_EAr$ reactions of pyrroles, see: Joule, J. A.; Mills, K. *Heterocyclic Chemistry*, 5th ed.; John Wiley & Sons: Chichester, 2010; pp 289–323.

(21) For other examples, see: (a) Dohi, T.; Yamaoka, N.; Kita, Y. *Tetrahedron* **2010**, *66*, 5775. (b) Reference 16. (c) Martin-Santamaria, S.; Carroll, M. A.; Carroll, C. M.; Carter, C. D.; Pike, V. W.; Rzepa, H. S.; Widdowson, D. A. *Chem. Commun.* **2000**, 649.

**Table 2.** Acetoxylation of Pyrroles **1a**–**k** and Indoles **1l**–**m** via Isolation of Intermediate Iodonium Salts **2a**–**m**



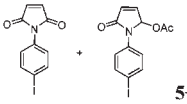
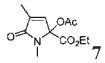
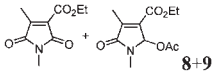
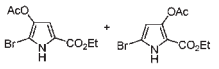

| entry | iodonium salt | time (h) | yield (%) | product | time (h) | yield[a] (%) |
|---|---|---|---|---|---|---|
| 1 |  **2a** | 6 | 78 |  **3a** | 18 | 90 |
| 2 |  **2b** | 3 | 77 |  **3b** | 1 | 85 |
| 3 |  **2c** | 6 | 72 |  **3c** | 3 | 79 |
| 4 |  **2d** | 3 | 79 |  **3d** | 3 | 78 |
| 5 |  **2e** | 6 | 65 |  **3e** | 18 | 79 |
| 6 |  **2f** | 3 | 79 |  **3f** | 18 | 71 |
| 7 |  **2g** | 18 | 63 |  **3g** | 18 | 73 |
| 8 |  **2h** | 18 | 73 |  **3h** | 18 | 79 |
| 9 |  **2i** | 3 | 71 |  **3i** | 18 | 67 |
| 10 |  **2j** | 18 | 71 |  **3j** | 18 | 71 |
| 11 |  **2k** | 18 | 79 |  **3k** | 1 | 74[b] |
| 12 |  **2l** | 18 | 79 |  **3l** | 1 | 81[b] |
| 13 |  **2m** | 6 | 66 |  **3m** | 3 | 73 |

[a] Yields for the conversion from **2** to **3**. [b] Heating at 100 °C.

were readily converted into the target acetoxypyrroles **3a**–**k** (see Table 2). A simple workup and purification by chromatography afforded pure **3a**–**k** (Table 2). The Pd-catalyzed acetoxylation conditions are compatible with the presence of bromine (entries 8, 11) and even iodine (entry 2). *N*-Alkyl, *N*-aryl, *N*-benzoyl, *N*-benzyl, *N*-tosyl, and *N*-carbamoyl are tolerated at the pyrrole nitrogen (Table 2).

We have found that the acetoxypyrroles **3a**–**k** could also be synthesized in a sequential one-pot approach without

**Table 3.** One-Pot Sequential Procedure vs Crabtree Conditions

| entry | pyrrole | One-pot[a] product | yield (%) | Crabtree conditions[b] product | yield (%) |
|---|---|---|---|---|---|
| 1 | **1a** | **3a** | 92 | **3a** | 85 |
| 2 | **1b** | **3b** | 56 |  **5**+**6** | 27 (**5**)[c] 41 (**6**)[c] |
| 3 | **1c** | **3c** | 80 |  **7** | 75[c] |
| 4 | **1d** | **3d** | 77 |  **8**+**9** | 34 (**8**)[c] 51 (**9**)[c] |
| 5 | **1e** | **3e** | 86 | **3e** | 76 |
| 6 | **1f** | **3f** | 60 | **3f** | 65 |
| 7 | **1g** | **3g** | 50 | - | - |
| 8 | **1h** | **3h** | 74 |  **3h**:**10**=4:1 | 74[d] |
| 9 | **1i** | **3i** | 42 | - | - |
| 10 | **1j** | **3j** | 41 | - | - |
| 11 | **1k** | **3k** | 69 | **3k** | 41[c,e] |
| 12 | **1l** | **3l** | 86 | **3l** | 77[f] |
| 13 | **1m** | **3m** | 70 | **3m** | 51 |

[a] Pyrrole **1** (1 equiv) and $PhI(OAc)_2$ (1.2 equiv) were stirred in AcOH at rt for 3–18 h (see Table 2 for time; the formation of **2** was monitored by $^1H$ NMR), then $Pd(OAc)_2$ (0.05 equiv) was added, and stirring at rt was continued for 1–18 h (see Table 2). [b] Pyrrole **1** (1 equiv), $PhI(OAc)_2$ (1.3 equiv), and $Pd(OAc)_2$ (0.05 equiv) were heated in AcOH at 100 °C for 1 h. [c] 2.3 equiv of $PhI(OAc)_2$. [d] Yield of a 4:1 mixture of **3h** and **10**. [e] Heating at 100 °C for 3 h. [f] Reference 5e.

isolation of the intermediate iodonium salts **2a**–**k** (see Table 3). Accordingly, $Pd(OAc)_2$ was added to the reaction mixture after the corresponding iodonium acetate has been formed.[22] In general, the sequential one-pot approach afforded higher yields of **3a**–**k** compared to the two-step reaction. Importantly, the original Crabtree[7] conditions are inferior to the sequential one-pot approach. Thus, not only the yields are substantially lower (Table 3, entries 1, 5, 8, 11, 12) but also the formation of overoxidation products is more pronounced. For example, acetoxylation of pyrroles **1b**–**d** under Crabtree conditions (entries 2–4, Table 3) afforded mixtures of pyrrole-2,5-diones **5,8** and 5-functionalized pyrrolidin-2-ones **6,7,9**. γ-Lactams such as **6,7,9** have been found in a wide range of biologically active natural products.[23]

The initial formation of salts **2a**–**k** in the Pd-catalyzed acetoxylation reaction prompted us to hypothesize that the previously reported acetoxylation of indoles under similar conditions ($Pd(OAc)_2$ and $PhI(OAc)_2$)[5e] may also proceed via the intermediate indolyliodonium acetates. Indeed, treatment of indoles **1l,m** with $PhI(OAc)_2$ in AcOH afforded C3-iodonium salts **2l,m** which were stable in AcOH-$d_4$ solution and could be isolated.[24]

(22) The formation of iodonium acetates **2a**–**k** was controlled by $^1H$ NMR. The addition of $Pd(OAc)_2$ early on resulted in the formation of overoxidation products.

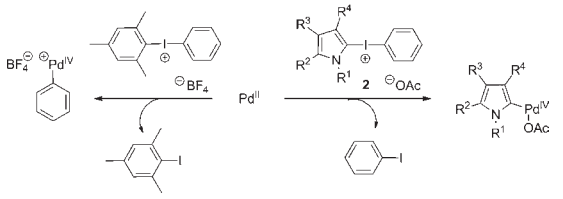
(23) For a review, see: Nay, B.; Riache, N.; Evanno, L. *Nat. Prod. Rep*. **2009**, *26*, 1044.

(24) The structures of **2a** and **2l** were confirmed by X-ray analysis; see the Supporting Information, pp S29 and S30.

Furthermore, salts **2l,m** were smoothly converted into acetoxyindoles **3l,m** in the presence of $Pd(OAc)_2$ (5 mol %) (see Table 2, entries 12, 13). The sequential one-pot approach afforded higher yields of **3l** compared to the Crabtree conditions (86% vs 77%, Table 3, entry 12).

The Pd-catalyzed formation of C−O bonds from iodonium acetates **2a**−**m** showed high regioselectivity for the sterically more bulky heterocycle ring, and *O*-acetylphenol formation was not observed. Assuming that acetoxylation occurs via the initial transfer of pyrroles and indoles from the iodonium salts **2** to Pd, the observed regioselectivity is striking, because the less hindered aryl group usually is transferred from nonsymmetrical diaryliodonium salts (such as [Ar-I-Mes]$BF_4$) to Pd (Scheme 1).[25]

**Scheme 1.** Regioselectivity in the Reaction of Nonsymmetrical Iodonium Salts with Palladium



Apparently, electronic preferences rather than steric factors control the acetoxylation regioselectivity of salts **2**. Thus, it has been demonstrated that in Pd(II)-catalyzed reactions the more electron-rich Ar moiety is selectively transferred from unsymmetrical diaryliodonium salts [Ar-I-Ar′]$BF_4$ to a Pd catalyst.[26,27] The high regioselectivity of the pyrrole and indole ring transfer to a Pd catalyst, presumably, is ensured by $\eta^2$-coordination of an iodonium substituted double bond of the more electron-rich pyrrolyliodonium moiety to the Pd(II) species (complex **11**, Scheme 2).[28] Subsequent oxidative addition would generate a transient pyrrolyl−Pd(IV)

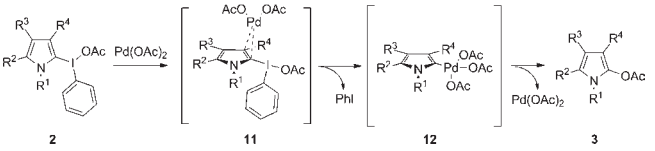
(25) The presence of a bulky mesityl group in iodonium salts [Mes-I-Ar]X ensured the selective transfer of the smaller Ar group in Pd-catalyzed arylations: (a) Kalyani, D.; Deprez, N. R.; Desai, L. V.; Sanford, M. S. *J. Am. Chem. Soc.* **2005**, *127*, 7330. (b) Deprez, N. R.; Sanford, M. S. *J. Am. Chem. Soc.* **2009**, *131*, 11234. For the analogous use of a nontransferrable 2,4,6-tri-isopropylphenyl group, see:Phipps, R. J.; Grimster, N. P.; Gaunt, M. J. *J. Am. Chem. Soc.* **2008**, *130*, 8172.

(26) Deprez, N. R.; Sanford, M. S. *Inorg. Chem.* **2007**, *46*, 1924 and references cited therein.

(27) Decomposition of [Mes-I-Ph]OAc under Crabtree acetoxylation conditions ($Pd(OAc)_2$, AcOH, 100 °C, 18 h) was moderately selective for the formation of Mes-OAc (ratio Mes-OAc/Mes-I = 3.4:1).

(28) (a) Related $\eta^2$-coordination of 2-tributylstannylfurane to Pd(II) followed by tin-to-palladium transmetallation of the furyl group has been observed: Cotter, W. D.; Barbour, L.; McNamara, K. L.; Hechter, R.; Lachicotte, R. J. *J. Am. Chem. Soc.* **1998**, *120*, 11016. (b) For related stable $\eta^2$-arylgold(I) complexes, see: Herrero-Gómez, E.; Nieto-Oberhuber, C.; Salomé, L.; Benet-Buchholz, J.; Echavarren, A. M. *Angew. Chem., Int. Ed.* **2006**, *45*, 5455.

**Scheme 2.** Proposed Mechanism for Acetoxylation of Pyrroles



complex **12**, which undergoes C−O bond forming reductive elimination.

The acetoxylation of pyrroles presumably involve a Pd(II)/Pd(IV) or Pd(II)/Pd(III) catalytic cycle. However, the Pd(0)/Pd(II) catalytic cycle cannot be ruled out, as evidenced by the "mercury drop" test.[29] Thus, addition of a large excess ( > 300 equiv) of metallic Hg to a mixture of iodonium acetate **2a** and $Pd(OAc)_2$ (5 mol %) in AcOH resulted in complete inhibition of the acetoxylation ( < 5% of acetoxypyrrole **3a** was formed).[30] Additional work is ongoing to elucidate the mechanism of the Pd-catalyzed conversion of **2** to **3**.

In summary, a series of stable pyrrolyl(aryl)iodonium and indolyl(aryl)iodonium acetates **2a**−**m** have been prepared and characterized. The formation of intermediate iodonium salts of pyrroles **2a**−**k** and indoles **2m,l** under the acetoxylation conditions as well as their Pd-catalyzed conversion to oxidized heterocycles **3a**−**l** indicate that iodonium salts **2a**−**l** are actual intermediates in the acetoxylation reaction. Consequently, we propose that the formation of iodonium salts **2** is the first step in the catalytic cycle for the acetoxylation of pyrroles and indoles. Such a mechanism differs from the closely related Pd-catalyzed C2-arylation of pyrroles and indoles with diaryliodonium salts, which proceeds via the initial carbopalladation of the pyrrole ring.[31] Further studies to expand the scope of heterocycles in the Pd-catalyzed regioselective acetoxylation reaction via iodonium acetates are ongoing in our laboratory.

**Acknowledgment.** This work was supported by the European Regional Development Fund (No. 2DP/2.1.1.1.0/10/APIA/VIAA/066).

**Supporting Information Available.** Experimental procedures, products characterization, copies of $^1H$ and $^{13}C$ NMR spectra, and X-ray crystallographic data for iodonium salts **2a,l** (CIF files). This material is available free of charge via the Internet at http://pubs.acs.org.

(29) (a) Anton, D. R.; Crabtree, R. H. *Organometallics* **1983**, *2*, 855. (b) Foley, P.; DiCosimo, R.; Whitesides, G. M. *J. Am. Chem. Soc.* **1980**, *102*, 6713.

(30) The formation of palladium black has always been observed in the late stages of the acetoxylation.

(31) Deprez, N. R.; Kalyani, D.; Krause, A.; Sanford, M. S. *J. Am. Chem. Soc.* **2006**, *128*, 4972.