

Supporting Information

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**Remarkably High Reactivity of Pd(OAc)<sub>2</sub>/Pyridine Catalysts:  
Nondirected C–H Oxygenation of Arenes\*\***

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## General Procedures

NMR spectra were recorded on a Varian MR 400 MHz NMR spectrometer with the residual solvent peak ([D<sub>2</sub>]dichloromethane: <sup>1</sup>H:  $\delta$ =5.32 ppm, <sup>13</sup>C:  $\delta$ =54.00 ppm) as the internal reference unless otherwise noted. Chemical shifts are reported in parts per million (ppm) ( $\delta$ ). Multiplicities are reported as follows: br (broad resonance), s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet). Coupling constants ( $J$ ) are reported in Hz. Infrared (IR) spectroscopy was performed on a Perkin Elmer FTIR. Peaks are reported in cm<sup>-1</sup> with the following relative intensities: s (strong, 67-100%), m (medium, 40-67%), w (weak, 20-40%), and br (broad). High resolution mass spectra were recorded on a Micromass AutoSpec Ultima Magnetic Sector mass spectrometer.

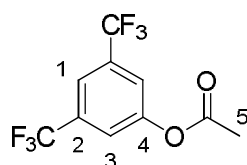
Reactions were conducted without rigorous exclusion of air and moisture unless noted otherwise. [D<sub>2</sub>]Dichloromethane and [D<sub>6</sub>]benzene were purchased from Cambridge Isotopes Lab and used as received. KBr for IR spectroscopy was purchased from Acros Organics. Dichloromethane (CH<sub>2</sub>Cl<sub>2</sub>), diethyl ether (Et<sub>2</sub>O), hexanes, and ethyl acetate (EtOAc) were obtained from Fisher Scientific or Aldrich and used as purchased. Benzene for acetoxylation and oxidative Heck reactions was obtained from Aldrich and stored over 4 Å molecular sieves. Celite and acetic anhydride were purchased from EM Science. PhBr, 3,5-bis(trifluoromethyl)phenol, and 2,6-lutidine were purchased from Acros Organics. PhCl, glacial acetic acid (AcOH), MgSO<sub>4</sub>, K<sub>2</sub>CO<sub>3</sub>, and triethylamine were purchased from Fisher Scientific. 1,2-Dichlorobenzene, iodomesitylene diacetate (MesI(OAc)<sub>2</sub>) and  $\alpha,\alpha,\alpha$ -trifluorotoluene were purchased from TCI America. Pd(OAc)<sub>2</sub> was purchased from Pressure Chemical Company. Iodosobenzene diacetate

(PhI(OAc)<sub>2</sub>) was obtained from Alfa Aesar. Ethyl benzoate, phenyl acetate, ethyl acrylate, pyridine, 2-picoline, 2,6-di-*tert*-butylpyridine, 1,3-bis(trifluoromethyl)benzene, and PhCH<sub>2</sub>C(CH<sub>3</sub>)<sub>3</sub> were purchased from Aldrich. Oxygen (extra dry) was purchased from Metro Wieding. Flash silica gel was purchased from Dynamic Adsorbents. Stock solutions of pyridine were prepared using volumetric glassware and all liquid reagents were dispensed by difference using gas-tight Hamilton syringes.

## Synthesis of Reference Samples of Aryl Acetate Products

Reference compounds for the acetoxylation [different isomers of acetoxy-bromobenzene, acetoxy-chlorobenzene, acetoxy-dichlorobenzene, acetoxy-(ethylbenzoate), acetoxy-(trifluoromethyl)-benzene, and acetoxy-bis(trifluoromethyl)benzene] were prepared according to literature procedures.<sup>[1]</sup> In all cases, the NMR characterization data for these compounds matched that reported in the literature.

### 1,3-Bis(trifluoromethyl)-5-acetoxybenzene<sup>[2]</sup>



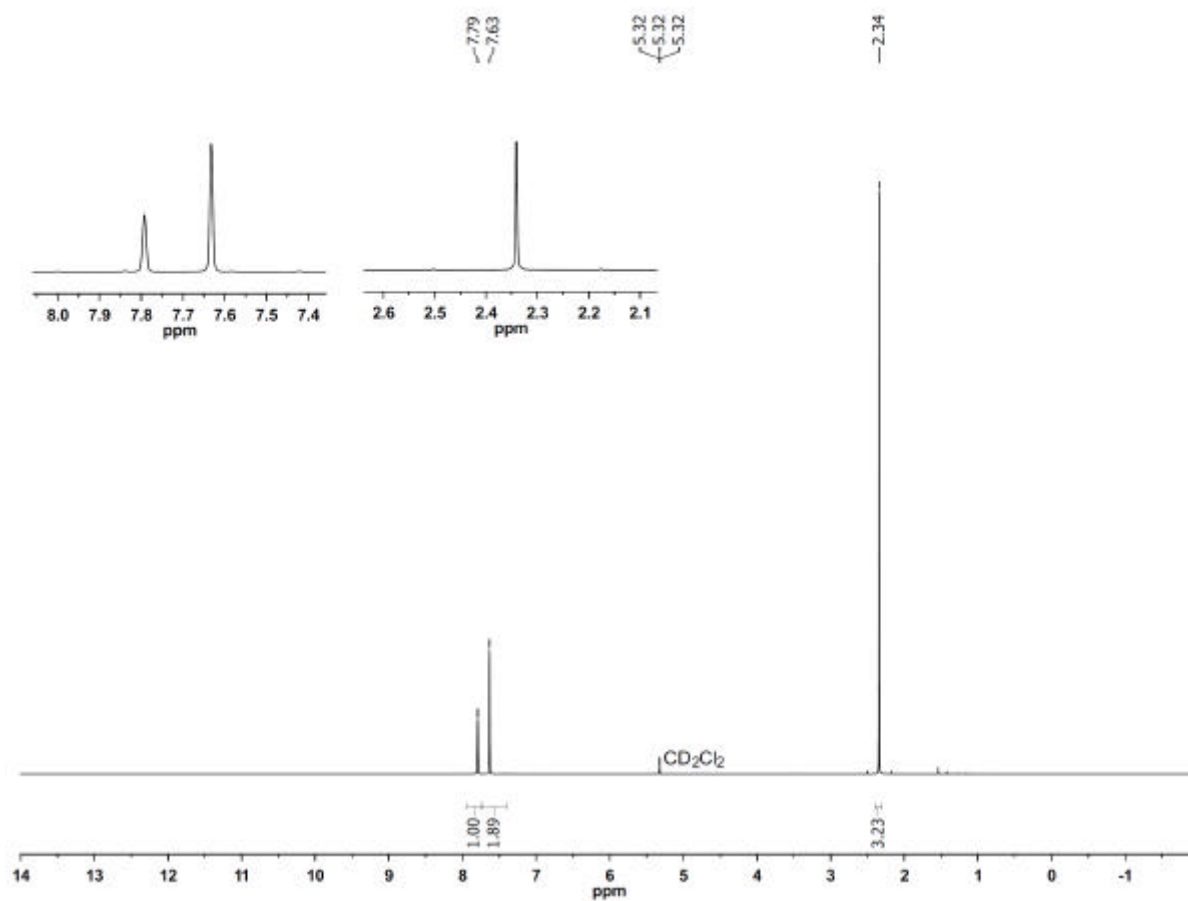
To a solution of 3,5-bis(trifluoromethyl)phenol (1.45 g, 6.31 mmol, 1.00 equiv) in CH<sub>2</sub>Cl<sub>2</sub> (6 mL), triethylamine (1.75 mL, 1.29 g, 12.6 mmol, 2.00 equiv), acetic anhydride (1.18 mL, 1.29 g, 12.6 mmol, 2.00 equiv), and AcOH (5 drops) were added sequentially at 0 °C. After complete addition, the ice bath was removed and the reaction mixture was stirred at RT for 14 h. The solution was poured into a mixture of H<sub>2</sub>O (50 mL) and CH<sub>2</sub>Cl<sub>2</sub> (50 mL), and stirred for 10 min. The phases were separated, and the aqueous phase was extracted twice with CH<sub>2</sub>Cl<sub>2</sub> (50 mL). The combined organic phases were dried over MgSO<sub>4</sub>, filtered, and the solvent was removed under reduced pressure. Column chromatography (gradient hexanes/CH<sub>2</sub>Cl<sub>2</sub> 49:1 to 4:1) afforded 1.16 g of 1,3-bis(trifluoromethyl)-5-acetoxybenzene (68% yield) as a colorless liquid. <sup>1</sup>H NMR (400 MHz, [D<sub>2</sub>]dichloromethane, 25 °C): *d*=7.79 (s, 1H; H-1), 7.63 (s, 2H; H-3), 2.34 (s, 3H; H-5);

[1] C. K. Lee; J. S. Yu; H.-J. Lee *J. Heterocycl. Chem.* **2002**, 39, 1207-1217.

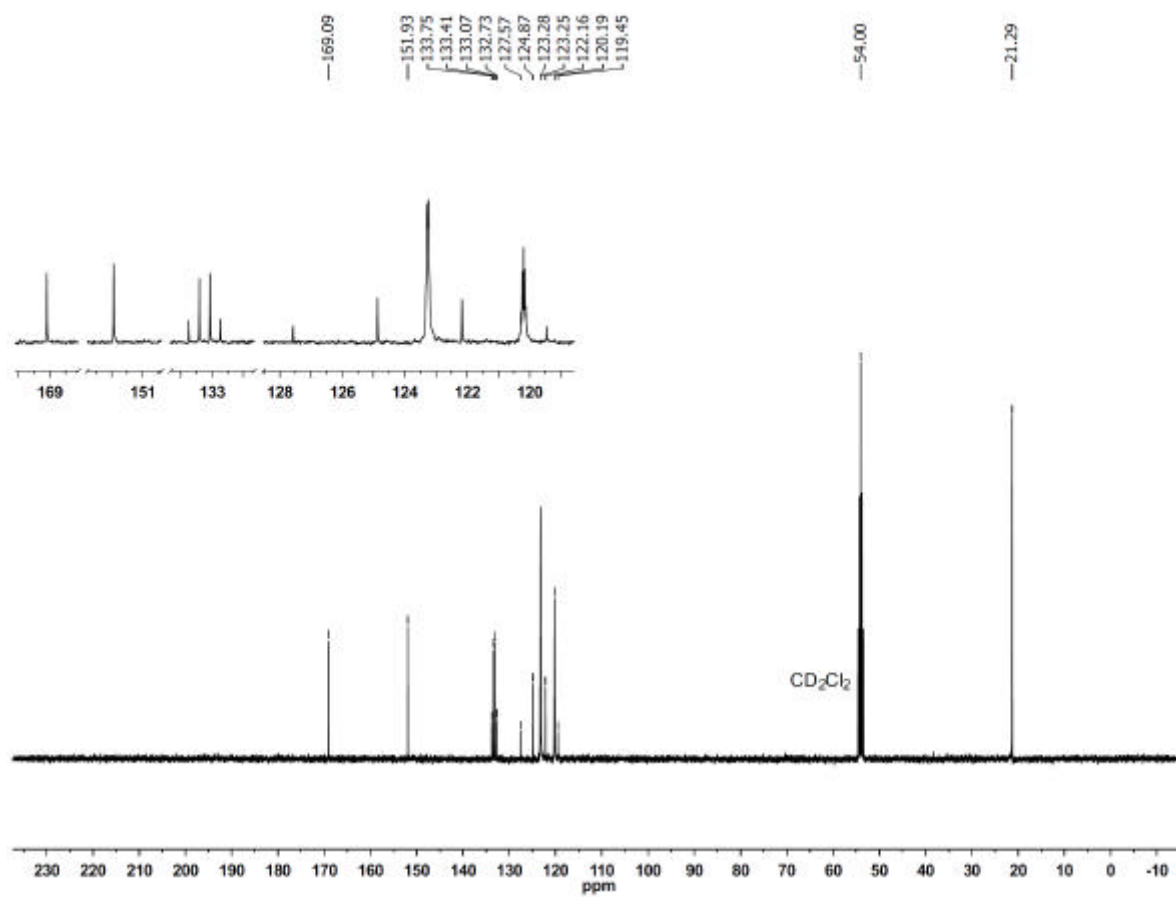
[2] Adapted from ref. [1].

$^{13}\text{C}$  NMR (100 MHz,  $[\text{D}_2]$ dichloromethane, 25 °C):  $\delta$ =169.1 (C=O), 151.9 (C-4), 133.2 (q,  $^2J(\text{C},\text{F})=33.9$  Hz; C-2), 123.5 (q,  $^1J(\text{C},\text{F})=272.7$  Hz;  $\text{CF}_3$ ), 123.3 (m, C-3), 120.2 (sept,  $^3J(\text{C},\text{F})=3.8$  Hz; C-1), 21.3 (C-5);  $^{19}\text{F}$  NMR (377 MHz,  $[\text{D}_2]$ dichloromethane, 25 °C):  $\delta$ =-63.4 (s); IR (KBr):  $\tilde{\nu}$ =3073 (w), 2919 (w), 2850 (w), 1779 (m), 1626 (w), 1464 (w), 1371 (s), 1282 (s), 1183 (br), 1137 (s), 1107 (w), 1015 (w), 954 (m), 899 (w), 858 (w), 740 (w), 701 (w), 683 (m), 588 (w), 536 (w)  $\text{cm}^{-1}$ ; HRMS (EI)  $m/z$ : 272.0281 [ $M^+$ ]; calc. for  $[\text{C}_{10}\text{H}_6\text{F}_6\text{O}_2^+]$ : 272.0272.

**Figure 1.**  $^1\text{H}$  NMR (400 MHz,  $[\text{D}_2]$ dichloromethane, 25 °C) of 1,3-bis(trifluoromethyl)-5-acetoxybenzene.

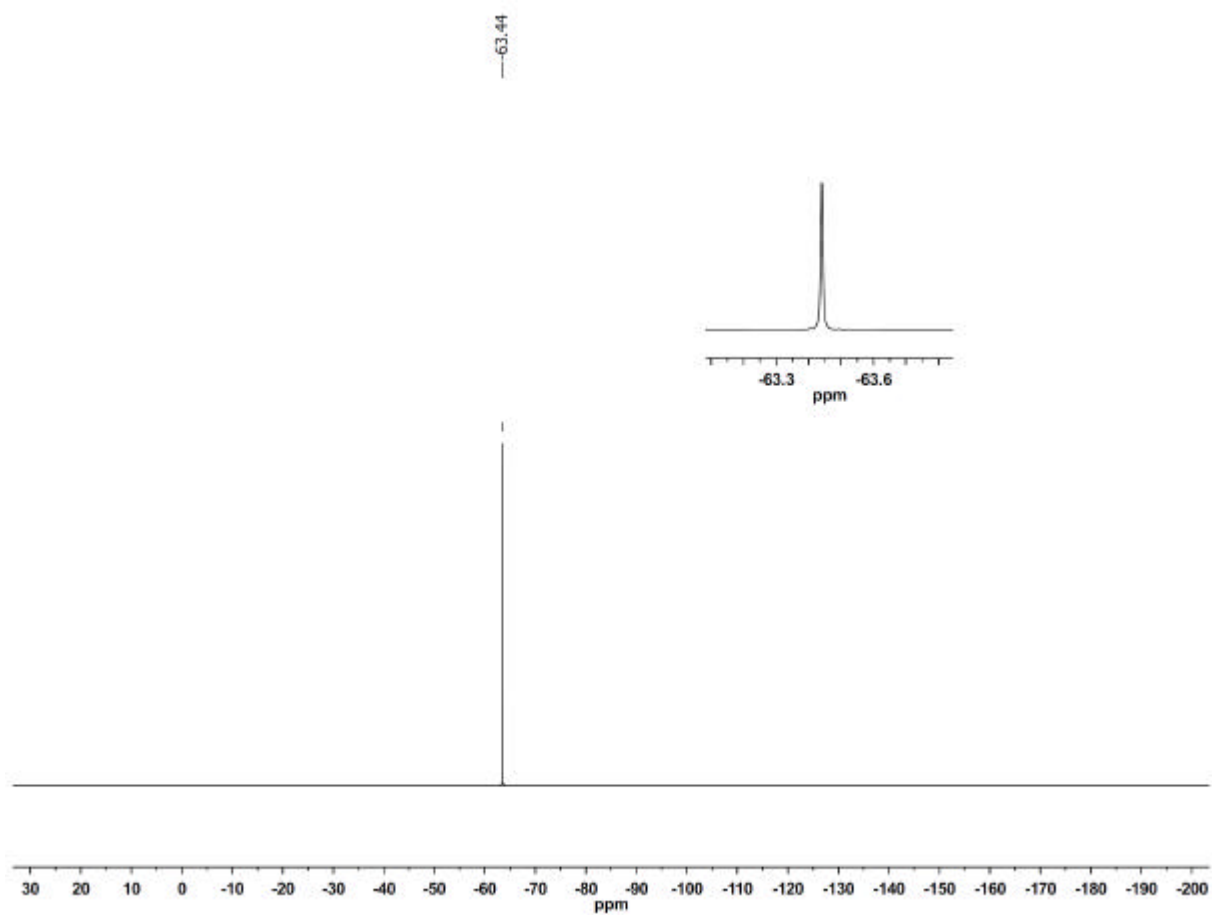


**Figure 2.**  $^{13}\text{C}$  NMR (100 MHz,  $[\text{D}_2]$ dichloromethane, 25  $^\circ\text{C}$ ) of 1,3-bis(trifluoromethyl)-5-acetoxybenzene.

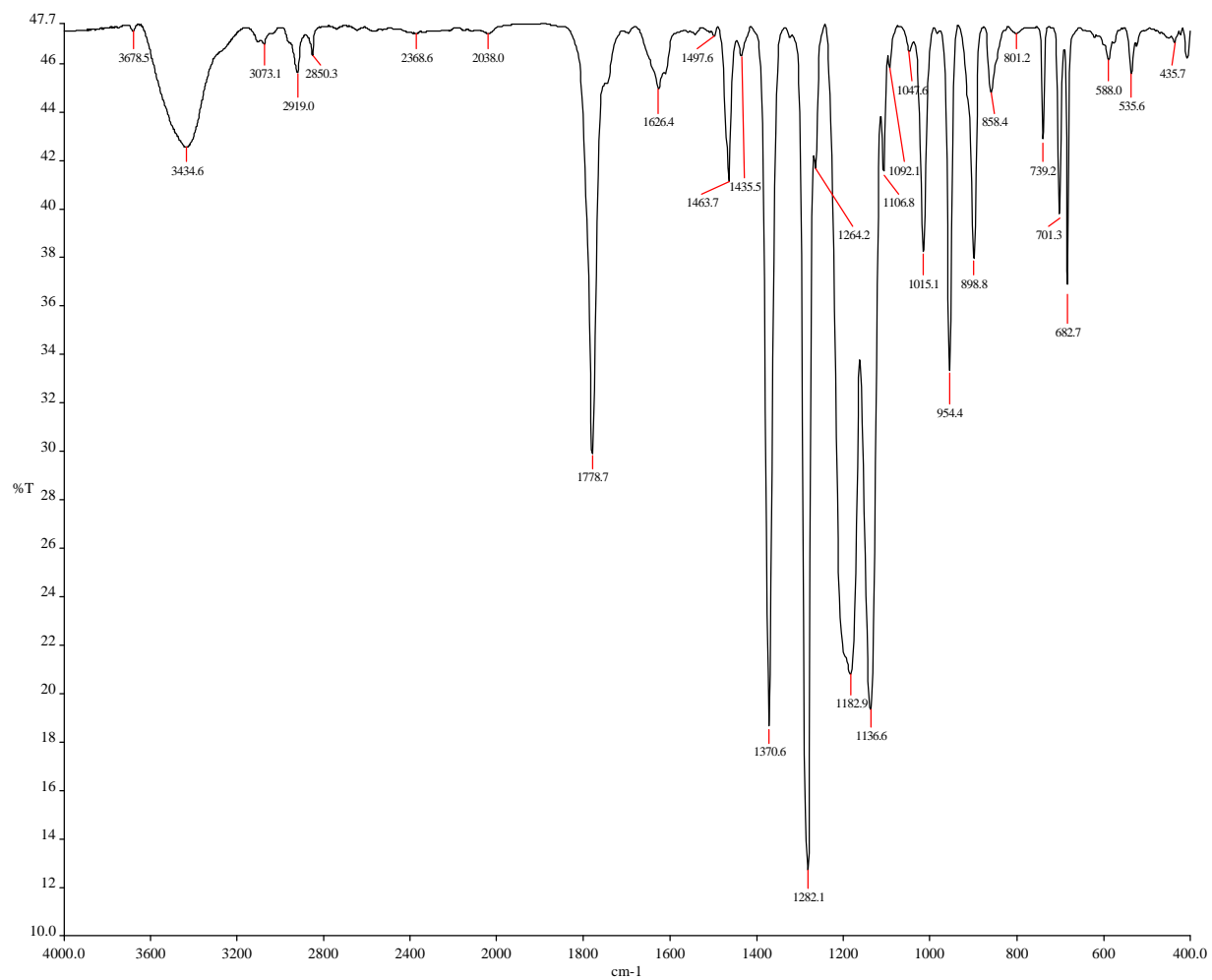




**Figure 3.**  $^{19}\text{F}$  NMR (377 MHz,  $[\text{D}_2]$ dichloromethane, 25 °C) of 1,3-bis(trifluoromethyl)-5-acetoxybenzene.



**Figure 4.** IR (KBr) of 1,3-bis(trifluoromethyl)-5-acetoxybenzene.



## Acetoxylation of Benzene - Time Studies

### General Procedure A. Pd(OAc)<sub>2</sub> catalyzed Acetoxylation of Benzene.<sup>[3]</sup>

PhI(OAc)<sub>2</sub> (361 mg, 1.12 mmol, 1.00 equiv) and Pd(OAc)<sub>2</sub> (5.0 mg, 22.4  $\mu$ mol, 2.0 mol %) were weighed into a pressure resistant vial. Glacial acetic acid (0.90 mL) and acetic anhydride (0.10 mL) were added. The resulting suspension was stirred at RT for 1 min, and then benzene (1.00 mL, 875 mg, 11.2 mmol, 10.0 equiv) was added. The vial was sealed with a Teflon-lined cap, and the reaction was heated to 100 °C using a preheated hotplate. At the end of the reaction, the vial was cooled to RT, and PhCl (20  $\mu$ L) was added as an internal standard for quantitative GC analysis. The reaction mixture was diluted with Et<sub>2</sub>O or EtOAc (2 mL) and filtered through a plug of Celite. The filtrate was extracted with a saturated aqueous solution of K<sub>2</sub>CO<sub>3</sub> (9 M in deionized H<sub>2</sub>O, 2 x 2 mL) to quench and separate the acid. The organic layer was then carefully separated and diluted with additional Et<sub>2</sub>O or EtOAc to a total volume of 20 mL. The resulting solution was analyzed by GC.

### General Procedure B. Pd(OAc)<sub>2</sub> catalyzed Acetoxylation of Benzene with Added Pyridine.

PhI(OAc)<sub>2</sub> (361 mg, 1.12 mmol, 1.00 equiv) and Pd(OAc)<sub>2</sub> (5.0 mg, 22.4  $\mu$ mol, 2.0 mol %) were weighed into a pressure resistant vial. 0.50 mL (22.4  $\mu$ mol, 2.0 mol %) of a stock solution of pyridine (36.2  $\mu$ L, 35.4 mg, 448  $\mu$ mol) in 10 mL AcOH, glacial acetic acid (0.40 mL) which had been prepared immediately prior to use, and acetic anhydride

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[3] Adapted from: T. Yoneyama; R. H. Crabtree *J. Mol Catal. A* **1996**, *108*, 35-40.

(0.10 mL) were added. The resulting suspension was stirred at RT for 1 min, and then benzene (1.00 mL, 875 mg, 11.2 mmol, 10.0 equiv) was added. The vial was sealed with a Teflon-lined cap, and the reaction was heated to 100 °C using a preheated hotplate. At the end of the reaction, the vial was cooled to RT, and PhCl (20 **nL**) was added as an internal standard for quantitative GC analysis. The reaction mixture was diluted with Et<sub>2</sub>O or EtOAc (2 mL) and filtered through a plug of Celite. The filtrate was extracted with a saturated aqueous solution of K<sub>2</sub>CO<sub>3</sub> (9 M in deionized H<sub>2</sub>O, 2 x 2 mL) to quench and separate the acid. The organic layer was then carefully separated and diluted with additional Et<sub>2</sub>O or EtOAc to a total volume of 20 mL. The resulting solution was analyzed by GC.

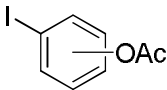
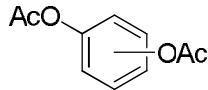
#### **Pd(OAc)<sub>2</sub> catalyzed Acetoxylation of Benzene - Addition of 4.0 mol % Pyridine**

By analogy to the General Procedure B (see above), PhI(OAc)<sub>2</sub> (361 mg, 1.12 mmol, 1.00 equiv), Pd(OAc)<sub>2</sub> (5.0 mg, 22.4 **n**mol, 2.0 mol %), 0.50 mL (44.8 **n**mol, 4.0 mol %) of a stock solution of pyridine (72.5 **nL**, 70.9 mg, 896 **n**mol) in 10 mL AcOH, AcOH (0.40 mL), acetic anhydride (0.10 mL) and benzene (1.00 mL, 875 mg, 11.2 mmol, 10.0 equiv) were reacted at 100 °C. Workup and analysis were performed as described above.

**Table 1.** Calibrated GC yields of phenyl acetate (PhOAc) in %. Conditions: benzene (1.00 mL, 875 mg, 11.2 mmol, 10.0 equiv), AcOH (0.90 mL), Ac<sub>2</sub>O (0.10 mL), PhI(OAc)<sub>2</sub> (361 mg, 1.12 mmol, 1.00 equiv), Pd(OAc)<sub>2</sub> (5.0 mg, 22.4  $\mu$ mol, 2.0 mol %), pyridine (0, 22.4 or 44.8  $\mu$ mol; 0, 2.0 or 4.0 mol %), 100 °C. The reported error is the standard deviation of at least two replicate trials.

Reaction Time [h]	Catalyst System		
	Pd(OAc) <sub>2</sub>	Pd(OAc) <sub>2</sub> /pyr 1:1	Pd(OAc) <sub>2</sub> /pyr 1:2
0.5	n.d.	12.7 ± 0.0	n.d.
1	n.d.	25 ± 2	n.d.
2	6.2 ± 0.0	63 ± 5	2 ± 1
3	n.d.	68 ± 1	n.d.
4	12.0 ± 0.1	68 ± 1	7 ± 2
6	17 ± 3	n.d.	n.d.
8	24 ± 4	68.3 ± 0.4	10 ± 3
12	33 ± 2	n.d.	n.d.
14	n.d.	68.6 ± 0.3	11 ± 4
16	51 ± 4	n.d.	n.d.
20	57 ± 3	68.1 ± 0.2	15 ± 4
24	66.2 ± 0.2	68.2 ± 0.2	14 ± 1

Yields are based on the oxidant PhI(OAc)<sub>2</sub> which has been shown to decompose upon

heating.<sup>[4]</sup> Observed byproducts include , , and biphenyl in accordance with ref. [3]. Both decomposition and formation of byproducts presumably contribute to the low yields (about 70%) upon complete conversion of the oxidant.

[4] J. E. Leffler; L. J. Story *J. Am. Chem. Soc.* **1967**, *89*, 2333-2338.

## Acetoxylation of Benzene – Pyridine Equivalent Studies

### **Pd(OAc)<sub>2</sub> catalyzed Acetoxylation of Benzene - Addition of 0-3.6 mol % Pyridine**

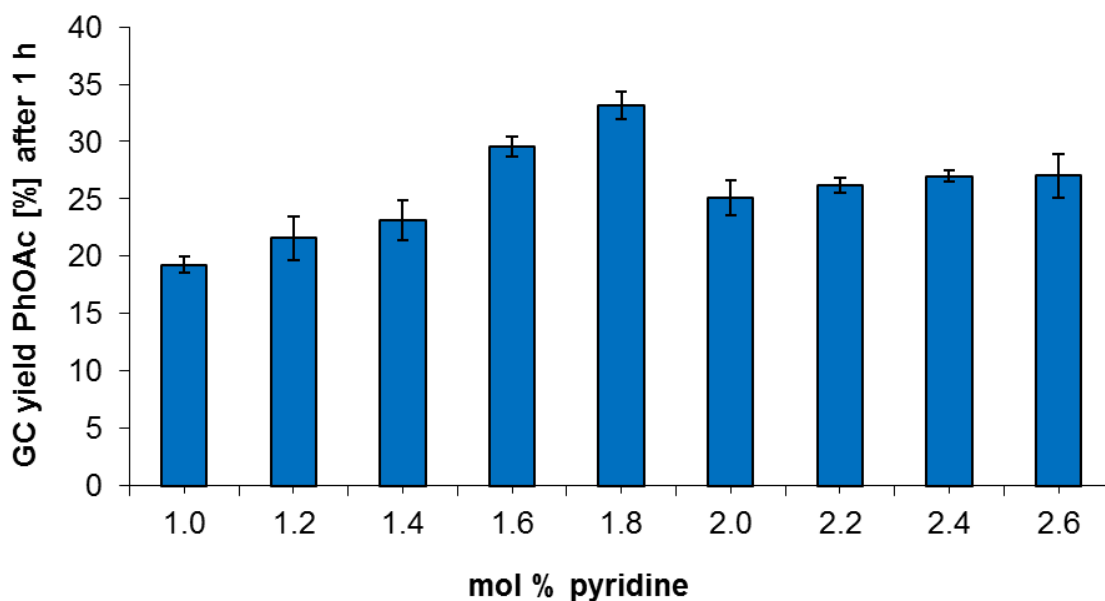
General Procedure B was followed using PhI(OAc)<sub>2</sub> (361 mg, 1.12 mmol, 1.00 equiv), Pd(OAc)<sub>2</sub> (5.0 mg, 22.4  $\mu$ mol, 2.0 mol %), x mL (see Table 2; 0 to 0.90 mL, 0 to 3.6 mol %) of a stock solution of pyridine (36.2  $\mu$ L, 35.4 mg, 448  $\mu$ mol) in 10 mL AcOH, AcOH (0.90-x mL, see Table 2), acetic anhydride (0.10 mL) and benzene (1.00 mL, 875 mg, 11.2 mmol, 10.0 equiv). Workup and analysis were performed as described above. Yields of PhOAc and exact amounts of AcOH and pyridine standard solution are listed in Table 2.

### **Pd(OAc)<sub>2</sub> catalyzed Acetoxylation of Benzene - Addition of 3.8-4.2 mol % Pyridine**

General Procedure B was followed using PhI(OAc)<sub>2</sub> (361 mg, 1.12 mmol, 1.00 equiv), Pd(OAc)<sub>2</sub> (5.0 mg, 22.4  $\mu$ mol, 2.0 mol %), x mL (see Table 3; 0.76 to 0.84 mL, 3.8 to 4.2 mol %) of a stock solution of pyridine (45.3  $\mu$ L, 44.2 mg, 560  $\mu$ mol) in 10 mL AcOH, AcOH (0.90-x mL, see Table 3), acetic anhydride (0.10 mL) and benzene (1.00 mL, 875 mg, 11.2 mmol, 10.0 equiv). Workup and analysis were performed as described above. Yields of PhOAc and exact amounts of AcOH and pyridine standard solution are listed in Table 3.

**Table 2.** Calibrated GC yields of phenyl acetate (PhOAc) in %. Conditions: benzene (1.00 mL, 875 mg, 11.2 mmol, 10.0 equiv), AcOH (0.90-x mL), Ac<sub>2</sub>O (0.10 mL), PhI(OAc)<sub>2</sub> (361 mg, 1.12 mmol, 1.00 equiv), Pd(OAc)<sub>2</sub> (5.0 mg, 22.4  $\mu$ mol, 2.0 mol %), x (0-0.90) mL stock solution of pyridine (36.2  $\mu$ L, 35.4 mg, 448  $\mu$ mol in 10 mL AcOH; 0.2-3.6 mol %), 100 °C, 1 or 2 h. The reported error is the standard deviation of at least two replicate trials.

(0.90-x) mL AcOH	x mL pyridine standard solution	mol % pyridine	Yield PhOAc 2 h (%)	Yield PhOAc 1 h (%)
0.90	0	0	6.2 $\pm$ 0.0	n.d.
0.85	0.05	0.2	33 $\pm$ 2	n.d.
0.80	0.10	0.4	36 $\pm$ 2	n.d.
0.75	0.15	0.6	38 $\pm$ 3	n.d.
0.70	0.20	0.8	57 $\pm$ 2	n.d.
0.65	0.25	1.0	612 $\pm$ 6	19 $\pm$ 1
0.60	0.30	1.2	63 $\pm$ 2	22 $\pm$ 2
0.55	0.35	1.4	66.0 $\pm$ 0.2	23 $\pm$ 2
0.50	0.40	1.6	67 $\pm$ 1	30 $\pm$ 1
0.45	0.45	1.8	66 $\pm$ 2	33 $\pm$ 1
0.40	0.50	2.0	63 $\pm$ 5	25 $\pm$ 2
0.35	0.55	2.2	63 $\pm$ 1	26 $\pm$ 1
0.30	0.60	2.4	65 $\pm$ 3	27 $\pm$ 1
0.25	0.65	2.6	67 $\pm$ 1	27 $\pm$ 2
0.20	0.70	2.8	56 $\pm$ 3	n.d.
0.15	0.75	3.0	39 $\pm$ 4	n.d.
0.10	0.80	3.2	33 $\pm$ 2	n.d.
0.05	0.85	3.4	30 $\pm$ 3	n.d.
0	0.90	3.6	14 $\pm$ 3	n.d.



**Figure 5.** Calibrated GC yields of phenyl acetate (PhOAc) after 1 h versus mol % pyridine. Conditions: benzene (1.00 mL, 875 mg, 11.2 mmol, 10.0 equiv), AcOH (0.90-x mL), Ac<sub>2</sub>O (0.10 mL), PhI(OAc)<sub>2</sub> (361 mg, 1.12 mmol, 1.00 equiv), Pd(OAc)<sub>2</sub> (5.0 mg, 22.4  $\mu$ mol, 2.0 mol %), x (0.25-0.65) mL stock solution of pyridine (36.2  $\mu$ L, 35.4 mg, 448  $\mu$ mol in 10 mL AcOH ; 1.0-2.6 mol %), 100 °C. The reported error is the standard deviation of at least two replicate trials.

**Table 3.** Calibrated GC yields of phenyl acetate (PhOAc) after 2 h in %. Conditions: benzene (1.00 mL, 875 mg, 11.2 mmol, 10.0 equiv), AcOH (0.90-x mL), Ac<sub>2</sub>O (0.10 mL), PhI(OAc)<sub>2</sub> (361 mg, 1.12 mmol, 1.00 equiv), Pd(OAc)<sub>2</sub> (5.0 mg, 22.4  $\mu$ mol, 2.0 mol %), x (0.76-0.84) mL stock solution of pyridine (45.3  $\mu$ L, 44.2 mg, 560  $\mu$ mol) in 10 mL AcOH; 3.8-4.2 mol %), 100 °C, 2 h. The reported error is the standard deviation of at least two replicate trials.

(0.90-x) mL AcOH	x mL pyridine standard solution	mol % pyridine	Yield PhOAc 2 h (%)
0.14	0.76	3.8	6 $\pm$ 3
0.10	0.80	4.0	2 $\pm$ 1
0.04	0.84	4.2	2 $\pm$ 1



## Acetoxylation of Benzene - Catalyst Loading Studies

### 0.50 mol % Pd(OAc)<sub>2</sub> / 0.45 mol % pyridine

General Procedure B was followed using PhI(OAc)<sub>2</sub> (1.44 g, 4.48 mmol, 1.00 equiv), Pd(OAc)<sub>2</sub> (5.0 mg, 22.4  $\mu$ mol, 0.50 mol %), 0.45 mL (0.45 mol %) of a stock solution of pyridine (36.2  $\mu$ L, 35.4 mg, 448  $\mu$ mol) in 10 mL AcOH, AcOH (3.15 mL), acetic anhydride (0.40 mL) and benzene (4.00 mL, 3.50 g, 44.8 mmol, 10.0 equiv). The reaction was heated at 100 °C for 15 h. After this time, Pd black formation was detected, indicating complete conversion of the oxidant. The GC yield of PhOAc was  $63.3 \pm 0.3$  %, corresponding to  $127 \pm 1$  turnovers.

### 0.10 mol % Pd(OAc)<sub>2</sub> / 0.09 mol % pyridine

General Procedure B was followed using PhI(OAc)<sub>2</sub> (1.44 g, 4.48 mmol, 1.00 equiv), Pd(OAc)<sub>2</sub> (1.0 mg, 4.48  $\mu$ mol, 0.10 mol %), 0.15 mL (0.09 mol %) of a stock solution of pyridine (21.7  $\mu$ L, 21.3 mg, 269  $\mu$ mol) in 10 mL AcOH, AcOH (3.45 mL), acetic anhydride (0.40 mL) and benzene (4.00 mL, 3.50 g, 44.8 mmol, 10.0 equiv). The reaction was heated at 100 °C for 23 h. After this time, Pd black formation was detected, indicating complete conversion of the oxidant. The GC yield of PhOAc was  $59.3 \pm 0.4$  %, corresponding to  $593 \pm 4$  turnovers.

### 0.01 mol % Pd(OAc)<sub>2</sub> / 0.009 mol % pyridine

General Procedure B was followed using PhI(OAc)<sub>2</sub> (4.33 g, 13.4 mmol, 1.00 equiv), 0.80 mL (1.34  $\mu$ mol, 0.01 mol %) of a stock solution of Pd(OAc)<sub>2</sub> (3.8 mg, 16.8  $\mu$ mol) in

10 mL benzene, 0.10 mL (1.21  $\mu$ mol, 0.009 mol %) of a stock solution of pyridine (9.8  $\mu$ L, 9.6 mg, 121  $\mu$ mol) in 10 mL AcOH, AcOH (10.7 mL), acetic anhydride (1.20 mL) and benzene (11.2 mL; total amount of benzene: 12.0 mL, 10.5 g, 134 mmol, 10.0 equiv). The reaction was heated at 100 °C for 306 h. After this time, Pd black formation was detected, indicating complete conversion of the oxidant. The GC yield of PhOAc was 48  $\pm$  2 %, corresponding to 4756  $\pm$  190 turnovers.

### Acetoxylation of Benzene – Addition of Second Charge of Oxidant

General Procedure B was followed using PhI(OAc)<sub>2</sub> (361 mg, 1.12 mmol, 1.00 equiv), Pd(OAc)<sub>2</sub> (5.0 mg, 22.4  $\mu$ mol, 2.0 mol %), 0.50 mL (20.2  $\mu$ mol, 1.8 mol %) of a stock solution of pyridine (32.6  $\mu$ L, 31.9 mg, 403  $\mu$ mol) in 10 mL AcOH, AcOH (0.40 mL), acetic anhydride (0.10 mL), and benzene (1.00 mL, 875 mg, 11.2 mmol, 10.0 equiv). The reaction was heated at 100 °C for 3 h. After this time, the vial was cooled with liquid nitrogen, and a second batch of PhI(OAc)<sub>2</sub> (361 mg, 1.12 mmol, 1.00 equiv) was added. The reaction was heated at 100 °C for 3.5 h. Workup and analysis were performed as described above. The GC yield of PhOAc for the second run was 54  $\pm$  2 %, assuming a yield of 66  $\pm$  2 % for the first run (which had been determined previously, see Table 2 above, entry 10).

## Substrate Scope of Acetoxylation using PhI(OAc)<sub>2</sub> as oxidant

### General procedure – Pd(OAc)<sub>2</sub>

General Procedure A was followed using PhI(OAc)<sub>2</sub> (361 mg, 1.12 mmol, 1.00 equiv), Pd(OAc)<sub>2</sub> (5.0 mg, 22.4  $\mu$ mol, 2.0 mol %), AcOH (0.90 mL), acetic anhydride (0.10 mL), and arene substrate (11.2 mmol, 10.0 equiv). Workup and analysis were performed as described above (for GC standards and exact amounts of aryl substrate, see Table 4). To obtain comparable data, in most cases the same reaction times were chosen as for the most active catalyst system (Pd(OAc)<sub>2</sub>/pyr 1:0.9); alternatively, reaction endpoints were determined by observation of Pd black formation which indicates complete conversion of the oxidant (see Table 6).



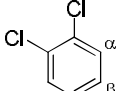


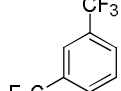
### General procedure – Pd(OAc)<sub>2</sub> / pyr 1:0.9

General Procedure B was followed using PhI(OAc)<sub>2</sub> (361 mg, 1.12 mmol, 1.00 equiv), Pd(OAc)<sub>2</sub> (5.0 mg, 22.4  $\mu$ mol, 2.0 mol %), 0.40 mL (20.2  $\mu$ mol, 1.8 mol %) of a stock solution of pyridine (40.8  $\mu$ L, 39.9 mg, 504  $\mu$ mol) in 10 mL AcOH, AcOH (0.50 mL), acetic anhydride (0.10 mL), and arene substrate (11.2 mmol, 10.0 equiv). Reaction endpoints were determined by observation of Pd black formation which indicates complete conversion of the oxidant (see Table 5). Workup and analysis were performed as described above (for GC standards and exact amounts of aryl substrate, see Table 4).

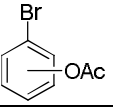
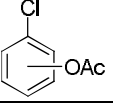
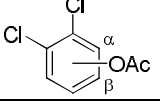
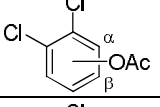
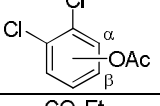
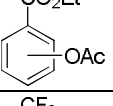
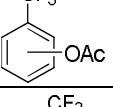
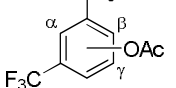
### General procedure – Pd(OAc)<sub>2</sub> / pyr 1:2.1

General Procedure B was followed using PhI(OAc)<sub>2</sub> (361 mg, 1.12 mmol, 1.00 equiv), Pd(OAc)<sub>2</sub> (5.0 mg, 22.4  $\mu$ mol, 2.0 mol %), 0.40 mL (47.0  $\mu$ mol, 4.2 mol %) of a stock solution of pyridine (95.1  $\mu$ L, 93.0 mg, 1176  $\mu$ mol) in 10 mL AcOH, AcOH (0.50 mL), acetic anhydride (0.10 mL), and arene substrate (11.2 mmol, 10.0 equiv). Workup and analysis were performed as described above (for GC standards and exact amounts of aryl substrate, see Table 4). To obtain comparable data, in most cases the same reaction times were chosen as for the most active catalyst system (Pd(OAc)<sub>2</sub>/pyr 1:0.9); alternatively, reaction endpoints were determined by observation of Pd black formation which indicates complete conversion of the oxidant (see Table 5).

**Table 4.** Amounts of Substrates used for Acetoxylation Substrate Scope and corresponding GC standards.

Substrate						
Amount used (11.2 mmol)	1.76 g, 1.18 mL	1.26 g, 1.14 mL	1.65 g, 1.26 mL	1.68 g, 1.60 mL	1.64 g, 1.38 mL	2.40 g, 1.74 mL
GC standard	PhCH <sub>2</sub> C(CH <sub>3</sub> ) <sub>3</sub>	PhCH <sub>2</sub> C(CH <sub>3</sub> ) <sub>3</sub>	PhCH <sub>2</sub> C(CH <sub>3</sub> ) <sub>3</sub>	PhCH <sub>2</sub> C(CH <sub>3</sub> ) <sub>3</sub>	PhCl	PhCl

**Table 5.** Calibrated GC yields and site selectivities of acetoxyated products in %. Conditions: substrate (11.2 mmol, 10.0 equiv), AcOH (0.50 mL), Ac<sub>2</sub>O (0.10 mL), PhI(OAc)<sub>2</sub> (361 mg, 1.12 mmol, 1.00 equiv), Pd(OAc)<sub>2</sub> (5.0 mg, 22.4  $\mu$ mol, 2.0 mol %), 0.40 mL stock solution of pyridine (504  $\mu$ mol in 10 mL AcOH; 1.8 mol % or 1176  $\mu$ mol in 10 mL AcOH; 4.2 mol %), 100 °C. The reported error is the standard deviation of at least two replicate trials.

Product	Reaction time	Oxidant	Yield Pd(OAc) <sub>2</sub> (o:m:p)	Yield Pd(OAc) <sub>2</sub> /pyr 1:0.9 (o:m:p)	Yield Pd(OAc) <sub>2</sub> /pyr 1:2.1 (o:m:p)
	5 h	PhI(OAc) <sub>2</sub>	8 ± 1 (38:34:28)	70 ± 1 <sup>a</sup> (23:46:31)	5 ± 1 (16:51:33)
	5 h	PhI(OAc) <sub>2</sub>	7.1 ± 0.2 (41:29:30)	62 ± 1 <sup>a</sup> (29:40:31)	2.6 ± 0.3 (11:51:37)
	8 h	PhI(OAc) <sub>2</sub>	8 ± 2 (α:β 41:59)	59 ± 3 <sup>a</sup> (α:β 29:71)	4 ± 1 (α:β 29:71)
	42 h	PhI(OAc) <sub>2</sub>	n.d.	n.d.	37 ± 1 <sup>a</sup> (α:β 21:79)
	114 h	PhI(OAc) <sub>2</sub>	64 ± 1 <sup>a</sup> (α:β 41:59)	n.d.	n.d.
	8 h	PhI(OAc) <sub>2</sub>	5 ± 1 (18:66:16)	68 ± 1 <sup>a</sup> (11:71:18)	3 ± 2 (17:65:18)
	18 h	PhI(OAc) <sub>2</sub>	5 ± 1 (8:70:22)	47.4 ± 0.0 <sup>a</sup> (1:78:21)	3 ± 1 (7:55:38)
	22 h	PhI(OAc) <sub>2</sub>	0.8 ± 0.1 (β:γ <1:99)	23.6 ± 0.2 <sup>a</sup> (β:γ <1:99)	3.3 ± 0.3 (β:γ <1:99)

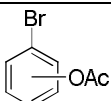
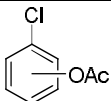
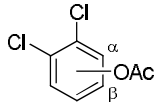
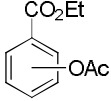
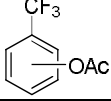
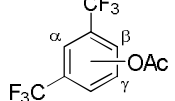
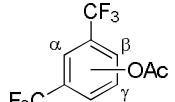
<sup>a</sup>Determined at complete conversion of the oxidant which is indicated by formation of Pd black in the reaction mixture.

## Substrate Scope of Acetoxylation using MesI(OAc)<sub>2</sub> as oxidant

### General procedure – Pd(OAc)<sub>2</sub> / pyr 1:0.9

General Procedure B was followed using iodomesitylene diacetate (408 mg, 1.12 mmol, 1.00 equiv), Pd(OAc)<sub>2</sub> (5.0 mg, 22.4  $\mu$ mol, 2.0 mol %), 0.40 mL (20.2  $\mu$ mol, 1.8 mol %) of a stock solution of pyridine (40.8  $\mu$ L, 39.9 mg, 504  $\mu$ mol) in 10 mL AcOH, AcOH (0.50 mL), acetic anhydride (0.10 mL), and arene substrate (11.2 mmol, 10.0 equiv). Reaction endpoints were determined by observation of Pd black formation which indicates complete conversion of the oxidant (for yields see Table 6). Workup and analysis were performed as described above (for GC standards and exact amounts of substrate, see Table 4 above).

**Table 6.** Calibrated GC yields and site selectivities of acetoxyated products in %. Yields are determined at complete conversion of the oxidant which is indicated by formation of Pd black in the reaction mixture. Conditions: Substrate (11.2 mmol, 10.0 equiv), AcOH (0.50 mL), Ac<sub>2</sub>O (0.10 mL), MesI(OAc)<sub>2</sub> (408 mg, 1.12 mmol, 1.00 equiv), Pd(OAc)<sub>2</sub> (5.0 mg, 22.4  $\mu$ mol, 2.0 mol %), 0.40 mL stock solution of pyridine (504  $\mu$ mol in 10 mL AcOH; 1.8 mol %), 100 °C. The reported error is the standard deviation of at least two replicate trials.

Product	Reaction time	Oxidant	Yield Pd(OAc) <sub>2</sub> /pyr 1:0.9 (o:m:p)
	9 h	MesI(OAc) <sub>2</sub>	70.4 ± 0.1 (11:53:36)
	10 h	MesI(OAc) <sub>2</sub>	68 ± 2 (16:46:38)
	12 h	MesI(OAc) <sub>2</sub>	64 ± 1 ( $\alpha$ : $\beta$ 11:89)
	21 h	MesI(OAc) <sub>2</sub>	70 ± 1 (10:72:18)
	17 h	MesI(OAc) <sub>2</sub>	61 ± 1 (<1:78:22)
	50 h	MesI(OAc) <sub>2</sub>	29 ± 1 ( $\beta$ : $\gamma$ 1:99)
	18 h	MesI(OAc) <sub>2</sub>	56 ± 2 <sup>[a]</sup> ( $\beta$ : $\gamma$ <1:99)

[a] 10 mol % Pd(OAc)<sub>2</sub> and 9 mol % pyridine was used as catalyst system.




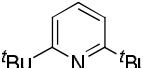


## Acetoxylation of 1,2-Dichlorobenzene – Influence of 2,6-Substitution of Pyridine-Type Additives on Site Selectivity

### General procedure

General Procedure B was followed using  $\text{PhI}(\text{OAc})_2$  (361 mg, 1.12 mmol, 1.00 equiv) or  $\text{MesI}(\text{OAc})_2$  (408 mg, 1.12 mmol, 1.00 equiv),  $\text{Pd}(\text{OAc})_2$  (5.0 mg, 22.4  $\mu\text{mol}$ , 2.0 mol %), 0.45 mL (20.2  $\mu\text{mol}$ , 1.8 mol %) of a stock solution of the additive (448  $\mu\text{mol}$ ) in 10 mL AcOH, AcOH (0.55 mL), acetic anhydride (0.10 mL), and 1,2-dichlorobenzene (1.26 mL, 1.65 g, 11.2 mmol, 10.0 equiv). Workup and analysis were performed as described above.

**Table 7.** Calibrated GC yields<sup>[a]</sup> of acetoxy-1,2-dichlorobenzene in %. Conditions: 1,2-dichlorobenzene (1.26 mL, 1.65 g, 11.2 mmol, 10.0 equiv), AcOH (0.55 mL), Ac<sub>2</sub>O (0.10 mL), ArI(OAc)<sub>2</sub> (1.12 mmol, 1.00 equiv), Pd(OAc)<sub>2</sub> (5.0 mg, 22.4  $\mu$ mol, 2.0 mol %), 0.45 mL stock solution of additive (448  $\mu$ mol in 10 mL AcOH; 1.8 mol %), 100 °C. The reported error is the standard deviation of at least two replicate trials.

Additive	Amount of 448 $\mu$ mol additive [mg, mL]	Reaction Time	Oxidant	Yield <sup>a</sup> ( $\alpha$ : $\beta$ Selectivity)
 Pyridine	35.4 mg, 36.2 mL	8 h	PhI(OAc) <sub>2</sub>	59 $\pm$ 3 (29:71)
Pyridine		12 h	MesI(OAc) <sub>2</sub>	64 $\pm$ 1 (11:89)
 2-Picoline	41.7 mg, 44.2 mL	20 h	PhI(OAc) <sub>2</sub>	74 $\pm$ 1 (35:65)
2-Picoline		20 h	MesI(OAc) <sub>2</sub>	76 $\pm$ 1 (14:86)
 2,6-Lutidine	48.0 mg, 52.2 mL	20 h	PhI(OAc) <sub>2</sub>	68 $\pm$ 2 (41:59)
2,6-Lutidine		27 h	MesI(OAc) <sub>2</sub>	71 $\pm$ 2 (21:79)
 2,6-Di- <i>tert</i> -butylpyridine	85.7 mg	120 h	PhI(OAc) <sub>2</sub>	64 $\pm$ 1 (38:62)
2,6-Di- <i>tert</i> -butylpyridine		52 h	MesI(OAc) <sub>2</sub>	44 $\pm$ 0 (31:69)
none	-	114 h	PhI(OAc) <sub>2</sub>	64 $\pm$ 1 (41:59)
none		68 h	MesI(OAc) <sub>2</sub>	51 $\pm$ 1 (29:71)




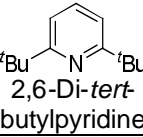
<sup>[a]</sup>Determined at complete conversion of the oxidant which is indicated by formation of Pd black in the reaction mixture.

## Acetoxylation of Benzene – Influence of 2,6-Substitution of Pyridine-Type Additives on the Reactivity of the Catalyst System

### General procedure

General Procedure B was followed using PhI(OAc)<sub>2</sub> (361 mg, 1.12 mmol, 1.00 equiv), Pd(OAc)<sub>2</sub> (5.0 mg, 22.4  $\mu$ mol, 2.0 mol %), 0.45 mL (20.2  $\mu$ mol, 1.8 mol %) of a stock solution of the additive (448  $\mu$ mol) in 10 mL AcOH, AcOH (0.55 mL), acetic anhydride (0.10 mL), and benzene (1.00 mL, 875 mg, 11.2 mmol, 10.0 equiv).

**Table 8.** Calibrated GC yields of phenyl acetate (PhOAc) after 1 and 2 h in %. Conditions: benzene (1.00 mL, 875 mg, 11.2 mmol, 10.0 equiv), AcOH (0.90 mL), Ac<sub>2</sub>O (0.10 mL), PhI(OAc)<sub>2</sub> (361 mg, 1.12 mmol, 1.00 equiv), Pd(OAc)<sub>2</sub> (5.0 mg, 22.4  $\mu$ mol, 2.0 mol %), 0.45 mL stock solution of additive (448  $\mu$ mol in 10 mL AcOH; 1.8 mol %), 100 °C. The reported error is the standard deviation of at least two replicate trials.

Additive	Amount of 448 $\mu$ mol additive [mg, mL]	Yield PhOAc 1 h (%)	Yield PhOAc 2 h (%)
 Pyridine	35.4 mg, 36.2 mL	33 $\pm$ 1	66 $\pm$ 2
 2-Picoline	41.7 mg, 44.2 mL	13.0 $\pm$ 0.2	25.9 $\pm$ 0.1
 2,6-Lutidine	48.0 mg, 52.2 mL	6 $\pm$ 1	14 $\pm$ 1
 2,6-Di- <i>tert</i> -butylpyridine	85.7 mg	2.8 $\pm$ 0.2	7.6 $\pm$ 0.0
none	-	2.4 $\pm$ 0.2	6.2 $\pm$ 0.0

## Kinetic Isotope Effect Studies

In contrast to the General Procedures A and B, all vials were frozen in liquid nitrogen directly after the end of the reaction and then stored at -30 °C until the workup was performed as described in General Procedures A and B.

### Pd(OAc)<sub>2</sub>

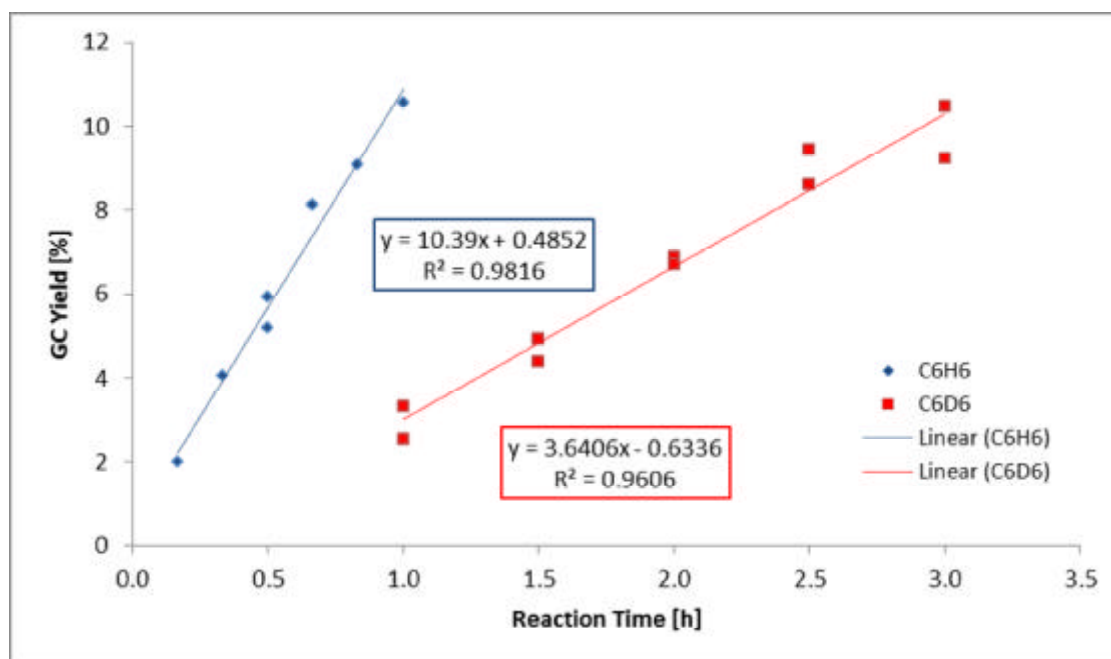
General Procedure A was followed using PhI(OAc)<sub>2</sub> (361 mg, 1.12 mmol, 1.00 equiv), Pd(OAc)<sub>2</sub> (5.0 mg, 22.4  $\mu$ mol, 2.0 mol %), AcOH (1.00 mL), acetic anhydride (0.10 mL), and benzene (1.00 mL, 875 mg, 11.2 mmol, 10.0 equiv) or [D<sub>6</sub>]benzene (0.99 mL, 942 mg, 11.2 mmol, 10.0 equiv).

**Table 9.** Calibrated GC yields of phenyl acetate using Pd(OAc)<sub>2</sub> as catalyst.

Reaction Time [h]	Yield PhOAc
0.17	2.00
0.33	4.07
0.50	5.94
0.50	5.18
0.67	8.13
0.83	9.09
1.00	10.57

**Table 10.** Calibrated GC yields of [D<sub>5</sub>]phenyl acetate using Pd(OAc)<sub>2</sub> as catalyst.

Reaction Time [h]	Yield PhOAc
1.00	2.53
1.00	3.31
1.50	4.39
1.50	4.93
2.00	6.87
2.00	6.71
2.50	8.59
2.50	9.45
3.00	9.22
3.00	10.47



**Figure 6.** Calibrated GC yields of PhOAc and [D<sub>5</sub>]PhOAc versus time and linear fit using Pd(OAc)<sub>2</sub> as catalyst.

### **Pd(OAc)<sub>2</sub>/pyr 1:0.9**

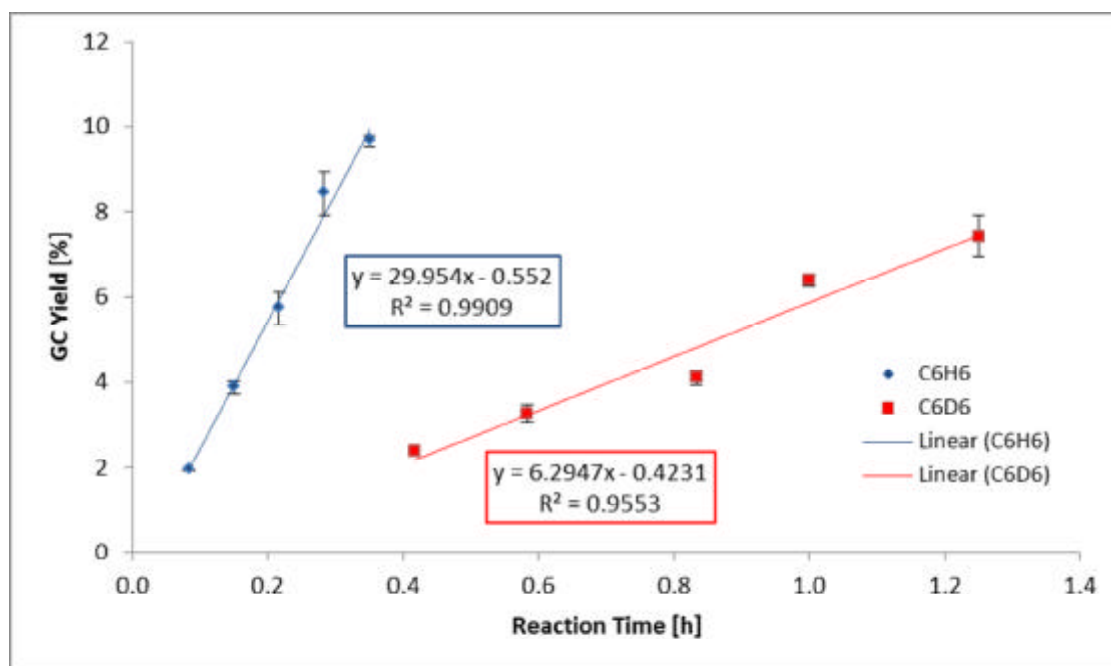
General Procedure B was followed using PhI(OAc)<sub>2</sub> (361 mg, 1.12 mmol, 1.00 equiv), Pd(OAc)<sub>2</sub> (5.0 mg, 22.4  $\mu$ mol, 2.0 mol %), 0.40 mL (20.2  $\mu$ mol, 1.8 mol %) of a stock solution of pyridine (40.8  $\mu$ L, 39.9 mg, 504  $\mu$ mol) in 10 mL AcOH, AcOH (0.50 mL), acetic anhydride (0.10 mL), and benzene (1.00 mL, 875 mg, 11.2 mmol, 10.0 equiv) or [D<sub>6</sub>]benzene (0.99 mL, 942 mg, 11.2 mmol, 10.0 equiv).

**Table 11.** Calibrated GC yields of phenyl acetate using Pd(OAc)<sub>2</sub>/pyr 1:0.9 as catalyst. The reported error is the standard deviation of at least two replicate trials.

Reaction Time [h]	Yield PhOAc
0.08	2.0 ± 0.0
0.15	3.9 ± 0.2
0.22	5.7 ± 0.4
0.28	8.4 ± 0.5
0.35	9.7 ± 0.1

**Table 12.** Calibrated GC yields of [D<sub>5</sub>]phenyl acetate using Pd(OAc)<sub>2</sub>/pyr 1:0.9 as catalyst. The reported error is the standard deviation of at least two replicate trials.

Reaction Time [h]	Yield PhOAc
0.42	2.4 ± 0.1
0.58	3.3 ± 0.2
0.83	4.1 ± 0.2
1.00	6.4 ± 0.1
1.25	7.4 ± 0.5



**Figure 7.** Calibrated GC yields of PhOAc and [D<sub>5</sub>]PhOAc versus time and linear fit using Pd(OAc)<sub>2</sub>pyr 1:0.9 as catalyst

### Pd(OAc)<sub>2</sub>/pyr 1:2.1

General Procedure B was followed using PhI(OAc)<sub>2</sub> (361 mg, 1.12 mmol, 1.00 equiv), Pd(OAc)<sub>2</sub> (5.0 mg, 22.4  $\mu$ mol, 2.0 mol %), 0.40 mL (47.0  $\mu$ mol, 4.2 mol %) of a stock solution of pyridine (95.1  $\mu$ L, 93.0 mg, 1176  $\mu$ mol) in 10 mL AcOH, AcOH (0.50 mL), acetic anhydride (0.10 mL), and benzene (1.00 mL, 875 mg, 11.2 mmol, 10.0 equiv) or [D<sub>6</sub>]benzene (0.99 mL, 942 mg, 11.2 mmol, 10.0 equiv).

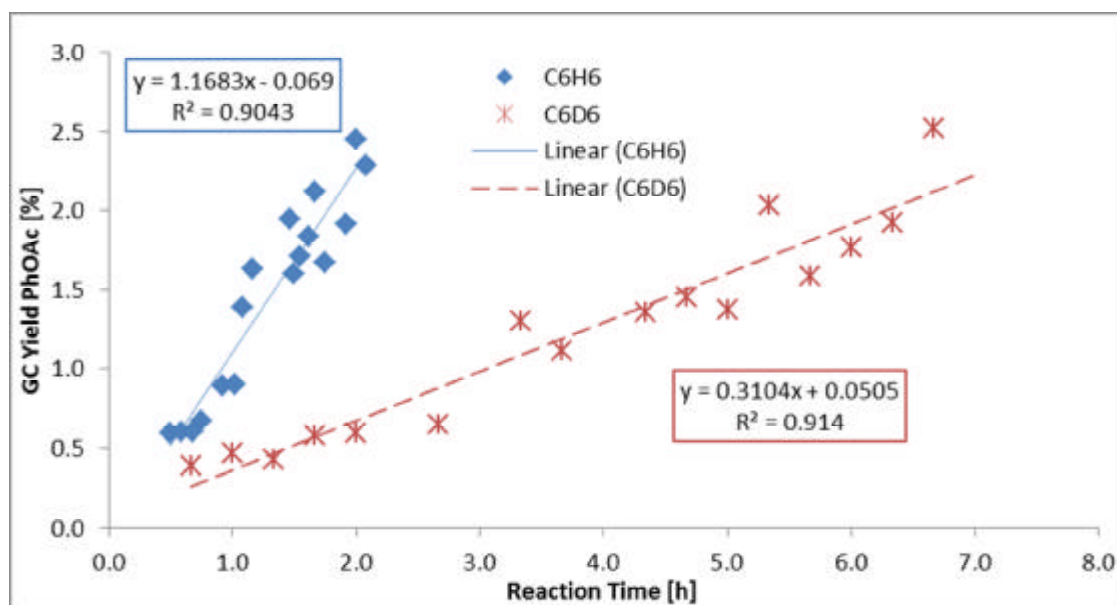
**Table 13.** Calibrated GC yields of phenyl acetate using Pd(OAc)<sub>2</sub>/pyr 1:2.1 as catalyst.

Reaction Time [h]	Yield PhOAc
0.50	0.59
0.58	0.60
0.68	0.60
0.75	0.68
0.92	0.89
1.02	0.90
1.08	1.39
1.17	1.64
1.47	1.94
1.50	1.60
1.55	1.71
1.62	1.84
1.67	2.12
1.75	1.67
1.92	1.92
2.00	2.45
2.08	2.28



**Table 14.** Calibrated GC yields of [D<sub>5</sub>]phenyl acetate using Pd(OAc)<sub>2</sub>/pyr 1:2.1 as catalyst.

Reaction Time [h]	Yield PhOAc
0.67	0.39
1.00	0.47
1.33	0.43
1.67	0.58
2.00	0.59
2.67	0.65
3.33	1.30
3.67	1.11
4.33	1.36
4.67	1.45
5.00	1.38
5.33	2.04
5.67	1.58
6.00	1.76
6.33	1.93
6.67	2.52



**Figure 8.** Calibrated GC yields of PhOAc and [D<sub>5</sub>]PhOAc versus time and linear fit using Pd(OAc)<sub>2</sub>/pyr 2.1 as catalyst