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Palladium-Catalyzed Aerobic Acetoxylation of Benzene using NO_x-Based Redox Mediators[‡]

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Abstract

Palladium-catalyzed methods for C–H oxygenation with O₂ as the stoichiometric oxidant are limited. Here, we describe the use of nitrite and nitrate sources as NO_x-based redox mediators in the acetoxylation of benzene. The conditions completely avoid formation of biphenyl as a side product, and strongly favor formation of phenyl acetate over nitrobenzene (PhOAc:PhNO₂ ratios up to 40:1). Under the optimized reaction conditions, with 0.1 mol% Pd(OAc)₂, 136 turnovers of Pd are achieved with only 1 atm of O₂ pressure.

Keywords

oxidation; aerobic; palladium; benzene; phenyl acetate; phenol; C–H activation; redox mediators; nitrate; nitrite; nitric acid

1. Introduction

Direct, selective oxidation of benzene to phenol and other oxygenates has been a major focus of attention in catalysis research [1], and palladium-catalyzed routes have shown significant promise [2]. Pd-catalyzed activation of an sp² C–H bond in benzene generates a phenyl-Pd^{II} species that can be trapped by various stoichiometric oxidants, such as PhI(OAc)₂ and persulfate, to afford phenyl-Pd^{III} or -Pd^{IV} species. These high-valent intermediates undergo facile C–O reductive elimination to afford phenyl acetate and related oxygenation products (Figure 1) [3], [4], [5]. The development of an effective method for benzene oxygenation capable of using O₂ as the oxidant remains a prominent challenge and goal of contemporary research [6].

Precedents for Pd-catalyzed oxygenation of benzene with O₂ as the oxidant are relatively limited [7], and the best examples typically require very high (unsafe) O₂ pressures. For example, Fujiwara disclosed Pd(OAc)₂/1,10-phenanthroline-catalyzed selective synthesis of

[‡]Dedicated to the memory of Alexander E. Shilov, an inspirational scientist who had a profound impact on the field of catalysis.

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phenol with O₂ in combination with CO as a sacrificial reductant [15 atm of each, turnover numbers (TON) = 12] [8]. Yin recently reported a Pd(OAc)₂/2,2'-bipyrimidine-catalyzed process using 20 atm of O₂, where selectivity was diverted from biphenyl to phenol when redox-inactive metals such as aluminum triflate were included in the reaction mixture (TON = 10.6) [9]. The most effective methods to date, however, employ Pd(OAc)₂ in combination with a heteropolyacid (HPA), H_{3+x}[PMo_{12-x}V_xO₄₀], cocatalyst. Schuchardt used a heteropolyacid with a vanadium content of x = 3.3 to achieve up to 600 Pd turnovers for phenol formation, although a very high O₂ pressure (60 atm) was required [10]. Kozhevnikov showed that a different HPA (x = 2) could shift the reaction from preferential biphenyl formation to phenol formation by increasing the water content in a H₂O:AcOH solvent mixture [11]. In this case, only modest turnovers (TON = 23) for phenol formation were observed, at 5 atm O₂. Finally, Ashland Oil patented the oxygenation of benzene with longer chain carboxylic acids. The reaction was performed in the presence of catalytic Pd(OAc)₂, Sb(OAc)₃ and Cr(OAc)₃ at a low pressure of O₂ (1 atm), achieving up to 90 turnovers with octanoic acid [12].

Pd-catalyzed oxidation of benzene under aerobic conditions typically affords biphenyl as the major reaction product [13]. A particular challenge in realizing a high-turnover process for benzene oxygenation is the typical inability of O₂ to react directly with phenyl-palladium(II) species to afford a high-valent species that can undergo facile C–O bond formation. Recently, well-defined organopalladium(II) complexes with multidentate ligands have been shown to react with O₂ to afford organopalladium(III) and/or organopalladium(IV) complexes [14], [15]; however, the specialized ligands used to achieve these transformations exhibit limited or no catalytic reactivity [16].

A number of historical and recent studies suggest that nitrogen oxide (NO_x) species [17] could serve as effective cocatalysts or stoichiometric mediators in aerobic palladium-catalyzed C–H oxidation reactions. For example, Bao recently used sodium nitrite as a cocatalyst to achieve aerobic trifluoroacetoxylation of methane [18] and Sanford used sodium nitrate as an additive in ligand-directed aerobic acetoxylation of sp³ C–H bonds [19]. Older precedents exist for application of similar concepts in the oxidation of benzene. In 1969, Tisue reported Pd(OAc)₂-catalyzed oxidation of benzene in the presence of sodium nitrite, leading to formation of nitrobenzene in preference to phenyl acetate (PhNO₂:PhOAc = 1.3:1; TON = 6, with respect to PhOAc) [20]. Asahi later published a patent in which they described preferential formation of phenyl acetate over nitrobenzene (PhOAc:PhNO₂ = 7:1; TON = 41, with respect to PhOAc) under modified conditions, most notably using a very high pressure of O₂ (19 atm) [21], [22]. More recently, NO_x-based reaction partners have been used in palladium-catalyzed, ligand-directed C–H nitration reactions [23]. Collectively, these results highlight the ability of NO_x species to promote carbon-heteroatom bond formation in Pd-catalyzed C–H oxidation; however, they also draw attention to potential challenges in controlling product selectivity.

(1)

(2)

In the present study, we explore the use of NO_x -based cocatalysts in the palladium-catalyzed aerobic oxidation of benzene to phenyl acetate. Of particular interest is the identification of reaction conditions that use low pressures of O_2 and achieve high selectivity for phenyl acetate relative to the potential by-products biphenyl and nitrobenzene (Figure 2).

2. Results and discussion

Our initial studies of palladium-catalyzed oxidation of benzene were carried out in the absence of NO_x sources in order to establish benchmarks for benzene reactivity with $\text{Pd}(\text{OAc})_2$. Benzene was dissolved in acetic acid (1:29 molar ratio) and heated to 100 °C in the presence of 1 mol% $\text{Pd}(\text{OAc})_2$ and 1 atm of O_2 . These conditions exhibited low conversion of benzene to oxidation products, resulting in 0.4 turnovers to biphenyl and phenol/phenyl acetate in a 1:1 ratio of C–O:C–C coupling products (Table 1, entry 1). A minor improvement was observed when $\text{Pd}(\text{OAc})_2$ was decreased to 0.1 mol% loading. The C–O coupling products were slightly favored over biphenyl (1.7:1); however, the overall reactivity still remained low (TON = 1.2). Negligible changes were observed when the O_2 partial pressure was increase to 10 atm (entry 3).

The latter results suggests that C–O coupling does not result from direct reaction of O_2 with a phenyl-palladium(II) intermediate and is consistent with previous observations that O_2 is kinetically inert toward direct reaction with organopalladium(II) species [24]. The origin of the small quantities of benzene oxygenation products in these reactions is not currently understood.

We then turned our attention to reactions incorporating NO_x -based cocatalysts (Table 2). When $\text{Pd}(\text{OAc})_2$ (1 mol%) was used with 10 mol% of *tert*-butyl nitrite as a NO_x source under 1 atm of O_2 , benzene oxidation exhibited a strong preference for phenyl acetate

formation over nitrobenzene and biphenyl side products, PhOAc:PhNO₂:Ph–Ph 10:1:0.8 (Table 2, entry 1; only trace phenol was detected). None of these oxidation products are observed if the same reaction is performed in the absence of Pd(OAc)₂. This observation shows that nitrobenzene formation is a palladium-catalyzed process and does not arise from electrophilic nitration under the reaction conditions. Recent mechanistic studies of palladium-catalyzed aerobic oxidative coupling of arenes revealed that biaryl formation proceeds via a bimetallic process involving transmetalation between two L_nPd^{II}ArX species [25]. Therefore, we conjectured that biphenyl formation could be minimized by reducing the catalyst loading. When the Pd(OAc)₂ and *tert*-butyl nitrite loadings were reduced to 0.1 and 1 mol%, respectively, no biphenyl was observed, and the TON with respect to PhOAc formation increased from 4 to 21. A similar PhOAc:PhNO₂ selectivity was observed (PhOAc:PhNO₂ = 8.4:1, entry 2). Increasing the O₂ partial pressure from 1 to 10 atm led to a slight increase in the palladium TON (26), but the PhOAc:PhNO₂ ratio improved to 27:1 (entry 3). Other changes to the reaction conditions, especially focused on the catalyst loading and identity of the NO_x source, did not lead to significant improvements (entries 4–9).

The active NO_x species appears to decompose under the reaction conditions, and addition of another dose of NO_x (in this case, *tert*-butyl nitrite) reinitiates the reaction [26]. This observation, together with the modest turnover numbers observed in Table 1 prompted us to investigate the use of larger quantities of NO_x sources for the reaction. In addition, we elected to focus on low- pressure reaction conditions (*p*O₂ = 1 atm).

Use of 30 mol% *tert*-butyl nitrite under 1 atm O₂, however, resulted in low catalyst turnover (Table 3, entry 1). We speculated that this poor result could reflect the deleterious consequence of generating larger quantities of *tert*-butoxyl radicals in the formation of NO from *tert*-butyl nitrite [27]. Therefore, other NO_x sources were tested. When 30 mol% NaNO₃ was employed, the turnover number increased to 59 and led to a PhOAc:PhNO₂ ratio of 9:1 (entry 2) [28]. Further improvements were observed upon using 30 mol% HNO₃ (70% in H₂O), which led to a turnover number of 115 (entry 3). The best results were obtained with 30 mol% fuming HNO₃, which led to a turnover number of 136 (entry 4). The selectivity for PhOAc over PhNO₂ remained very good under these conditions (PhOAc:PhNO₂ = 26:1, entry 4), in spite of the presence of a large quantity of NO_x. Only traces of diacetoxyated products were detected, even when the yield of PhOAc surpasses 10%. Varying the mol% of fuming HNO₃ led to modest reductions in turnover number (entries 5–7). When the optimized conditions, with 30 mol% fuming nitric acid, were conducted under N₂ instead of O₂, nitrobenzene is the major product (PhOAc:PhNO₂ = 1:1.2; entry 7). This result shows that the NO_x species can serve as competent oxidants, but they favor C–N bond formation, rather than C–O bond formation in the absence of O₂. The optimized conditions in Table 3, entry 4 afford a 13.6% yield of phenyl acetate, which compares favorably to previous methods for palladium-catalyzed oxidation of benzene to phenyl acetate using PhI(OAc)₂ and potassium persulfate as stoichiometric oxidants (7.5% [5a] and 7.1% [5f] yields, respectively). Additionally, the optimized conditions from entry 4 can be conducted under 1 atm of air instead of O₂, adjusting the temperature to 85 °C, to

afford a still high turnover number of 120, while the PhOAc:PhNO₂ ratio improved to 40:1 (entry 9).

A likely catalytic cycle for Pd(OAc)₂/NO_x-catalyzed oxidation of benzene to phenyl acetate is illustrated in Figure 3. Benzene C-H activation by palladium(II) [L_nPd(OAc)₂] affords a phenyl-palladium(II) intermediate. Two-electron oxidation of **1** by NO₂ could then generate a phenyl-palladium(IV) species **2**, which can undergo facile C–O reductive elimination to afford phenyl acetate and the original L_nPd(OAc)₂ catalyst. This proposed catalytic cycle mirrors other proposed Pd^{II/IV} (and Pd^{II}/Pd^{III} dimer) cycles for arene and alkane oxygenation, in which various oxidants (e.g. PhI(OAc)₂) are used to generate species similar to **2** [3a]. The proposed catalytically relevant oxidant NO₂ can be generated via thermal decomposition of HNO₃ (eq 3) [29], and the reduced NO_x species NO is well known to undergo facile aerobic oxidation to NO₂ [17].

The direct involvement of NO₂ (or other NO_x species) in oxidizing the phenyl-palladium(II) intermediate is supported by the observation of significant catalytic turnover (TON = 19), when the reaction is carried out in the absence of O₂. Furthermore, increased formation of nitrobenzene under these conditions (together with the lack of background nitration in the absence of palladium) implicates *N*-coordination of a NO_x species to palladium, which then participates in C–N reductive elimination. The change in PhOAc:PhNO₂ product selectivity under N₂ suggests that O₂ plays a role beyond oxidation of NO to NO₂.

In Table 2, increasing the O₂ pressure resulted in an improvement of the PhOAc:PhNO₂ ratio from 8.4:1 to 27:1 (entries 2 vs 3). Similarly, in Table 3, altering the reaction conditions from an O₂ to a N₂ atmosphere (1 atm in each case), significantly decreased the PhOAc:PhNO₂ product ratio from 26:1 to 1:1.2 (entries 4 vs 8) [30]. The reaction of NO_x species with organopalladium complexes has received relatively little attention, but fundamental studies of Campora and coworkers potentially provide insights into the selectivity trends just noted [31]. A nitrosyl-organopalladium(IV) complex bearing a tris(pyrazolyl)borate ancillary ligand (**3**) was synthesized and shown to react with O₂ to afford the corresponding *O*-bound nitrate complex **4** (Figure 4). Anaerobic conditions could result in accumulation of NO, which could then coordinate to organopalladium species and lead to C–N bond formation (the details of which are not yet understood). In the presence of O₂, nitric oxide could convert to NO₂ via direct oxidation by molecular oxygen, as shown in Figure 3, or a bound nitrosyl ligand could undergo oxidation to a nitrate ligand within the palladium coordination sphere, as shown in Figure 4. Either pathway could result in preferential C–O reductive elimination with a more-basic acetate ligand (cf. Figure 3).

3. Conclusions

In conclusion, we have demonstrated that NO_x sources serve as effective redox mediators for palladium-catalyzed aerobic acetoxylation of benzene under only 1 atm of O₂. Promising turnover numbers of >100 and high selectivities for phenyl acetate have been achieved.

Biphenyl formation is negligible under these reaction conditions, and phenyl acetate to nitrobenzene ratios of up to 40:1 are accessible.

4. Experimental

General considerations

The following reagents were purchased and used as received: benzene (Aldrich, anhydrous, 100-mL sure-seal bottles), acetic acid (Aldrich, >99.99%, trace metals basis), nitric acid (Aldrich, red fuming), palladium(II) acetate (Strem). The use of these high-purity reagents is **extremely important** in order to achieve optimal results. All reactions using 1 atm of pure O₂ were carried out in oven-dried Ace pressure tubes (9 mL, bushing type, front seal, 20.3 cm L x 13 mm O.D.). All reactions using 9% O₂/N₂ were carried out in a Series 5000 Multiple Reactor System (Parr Instrument Company) using 45-mL Hastelloy C-276 vessels. GC analyses were carried out on a Shimadzu Gas Chromatograph GC-1010 Plus, with a Phenomenex Zebtron ZB-Wax column (30 m L x 0.25 mm ID x 0.25 µm df).

Note: 1) It is important that the ratio of solution:headspace for these reactions be between 1:1.8 and 1:3.5 in order to achieve optimal results. 2) Because NO_x species will react with rubber, it is important that teflon caps, and not septa, be used for these reactions.

Reactions were optimized with respect to temperature, concentration, and ratio of solution:headspace (not shown).

Table 1: General procedure

A 45-mL Hastelloy C-276 vessel was charged with a teflon stirbar, the specified mol% of Pd(OAc)₂, as indicated in Table 2 (it is easiest to use a stock solution of Pd(OAc)₂/AcOH), a total of 12.1 mL of AcOH, and benzene (626 µL, 7 mmol). The reactor was sealed, pressurized to either 11 atm or 111 atm of 9% O₂/N₂ (effectively 1 atm of O₂ or 10 atm of O₂), and then heated to 100 °C and stirred vigorously for 10 h. The vessel was then allowed to cool to room temperature and the reaction mixture was analyzed by GC analysis using chlorobenzene as an internal standard. TONs are reported based on mmol PhOAc + mmol PhOH + mmol Ph–Ph. Ratios of (PhOAc + PhOH):Ph–Ph are based on mmol of products.

Table 2, entries 1 & 2: General procedure

An oven-dried Ace pressure tube (9 mL, bushing type, front seal, 20.3 cm L x 13 mm O.D.) was charged with a teflon stirbar, the specified mol% of Pd(OAc)₂ as indicated in Table 2 (it is easiest to use a stock solution of Pd(OAc)₂/AcOH), and a total of 3.0 mL of AcOH. The tube was capped with a septum and purged for 2 minutes with an oxygen balloon, while stirring. Benzene (158 µL, 1.75 mmol) was added via syringe, followed by the specified quantity of the NO_x source. The rubber septum was removed, quickly capped with a Teflon cap, and stirred vigorously in a 100 °C oil bath for 10 h (the oil bath level is the same height as the solution level of the reaction). The pressure tube was then allowed to cool to room temperature and the reaction mixture was analyzed by GC analysis using chlorobenzene as an internal standard. TONs are reported solely based on mmol PhOAc. Ratios of PhOAc:PhNO₂ are based on mmol of products.

Table 2, entries 3–9: General procedure

A 45-mL Hastelloy C-276 vessel was charged with a teflon stirbar, the specified mol% of $\text{Pd}(\text{OAc})_2$ as indicated in Table 2 (it is easiest to use a stock solution of $\text{Pd}(\text{OAc})_2/\text{AcOH}$), a total of 12.1 mL of AcOH, benzene (626 μL , 7 mmol), and the specified quantity of the NO_x source. The reactor was sealed, pressurized to 111 atm of 9% O_2/N_2 , and then heated to 100 $^\circ\text{C}$ and stirred vigorously for 10 h. The vessel was then allowed to cool to room temperature and the reaction mixture was analyzed by GC analysis using chlorobenzene as an internal standard. TONs are reported solely based on mmol PhOAc. Ratios of PhOAc:PhNO₂ are based on mmol of products.

Table 3: General procedure

An oven-dried Ace pressure tube (9 mL, bushing type, front seal, 20.3 cm L $\times$ 13 mm O.D.) was charged with a teflon stirbar, 100 μL of a 0.00012 M $\text{Pd}(\text{OAc})_2/\text{AcOH}$ stock solution (stock solution: 26.9 mg in 10 mL of AcOH; 0.0012 mmol $\text{Pd}(\text{OAc})_2$ per reaction), and 1.9 mL of AcOH. The tube was capped with a septum and purged for 2 minutes with an oxygen balloon, while stirring (exception: for entry 8, N_2 was used in place of O_2). Benzene (108 μL , 1.2 mmol) was added via syringe, followed by the specified quantity of the NO_x source, via syringe. The rubber septum was removed, quickly capped with a Teflon cap, and stirred vigorously in a 100 $^\circ\text{C}$ oil bath for 24 h (the oil bath level is the same height as the solution level of the reaction). The pressure tube was then allowed to cool to room temperature and the reaction mixture was analyzed by GC analysis using chlorobenzene as an internal standard. TONs are reported solely based on mmol PhOAc. Ratios of PhOAc:PhNO₂ are based on mmol of products.

*Entry 4 is the average of 4 runs:

Run 1: TON = 137; 28:1 PhOAc:PhNO₂

Run 2: TON = 136; 26:1 PhOAc:PhNO₂

Run 3: TON = 121; 30:1 PhOAc:PhNO₂

Run 4: TON = 149; 21:1 PhOAc:PhNO₂

Standard deviation for TON: 9.9

Standard deviation for PhOAc:PhNO₂ ratio: 3.3

Table 3, entry 9: Procedure

An oven-dried 100-mL round-bottom flask was charged with a teflon stirbar, 500 μL of a 0.027 M $\text{Pd}(\text{OAc})_2/\text{AcOH}$ stock solution (stock solution: 30.4 mg in 5 mL of AcOH; 0.0136 mmol $\text{Pd}(\text{OAc})_2$ per reaction), AcOH (22.7 mL), benzene (1.21 mL, 13.56 mmol), and fuming HNO_3 (173 μL , 4.07 mmol). The flask was equipped with a reflux condenser (open top) and stirred vigorously in a 85 $^\circ\text{C}$ oil bath for 24 h. The mixture was then allowed to cool to room temperature and the reaction mixture was analyzed by GC analysis using chlorobenzene as an internal standard. TONs are reported solely based on mmol PhOAc. Ratios of PhOAc:PhNO₂ are based on mmol of products.

Note: In a more rigorous approach for reactions run in Ace pressure tubes, Ace pressure tubes with plunger valves (e.g. Ace glass manufacturer #8648-164) were used. In this case, a pressure tube was charged with a Teflon stirbar, Pd(OAc)₂, AcOH, PhH and the NO_x source. The tube was sealed with a Teflon cap containing a plunger valve. The top of the plunger valve was connected to a three-way valve; one valve connected to a vacuum pump, and one valve connected to an O₂ balloon. The reaction mixture was frozen using a dry ice bath, evacuated under reduced pressure with the plunger valve open, and then backfilled with 1 atm of pure O₂. The plunger valve was closed and the reaction mixture was allowed to warm to room temperature. This evacuation/backfilling with O₂ procedure was conducted two more times, and then the sealed reaction mixture was stirred vigorously in a 100 °C oil bath for the indicated time. The pressure tube was then allowed to cool to room temperature and the reaction mixture was analyzed by GC analysis using chlorobenzene as an internal standard. Results using this approach were comparable to the less rigorous approach using Ace pressure tubes with simple Teflon caps.

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30. Note: the reaction conducted under N_2 is not completely devoid of O_2 , as O_2 is generated via HNO_3 thermal decomposition: $4 HNO_3 \rightarrow 2 H_2O + 4 NO_2 + O_2$.
31. Campora J, Palma P, del Rio D, Carmona E, Graiff C, Tiripicchio A. Organometallics. 2003; 22:3345–3347.

- Pd-catalyzed aerobic oxidation of benzene in acetic acid to phenyl acetate is enabled by the inclusion of NO_x-based redox mediators, achieving up to 136 turnovers.
- Phenyl acetate is strongly favored over the formation of the side product nitrobenzene (PhOAc:PhNO₂ ratios up to 40:1), and the potential byproduct biphenyl is not observed.
- High pressures of O₂ are not required; good reactivity is observed with air as the source of O₂.

Figure 1.
General proposed reaction mechanism for palladium-catalyzed benzene C–H acetoxylation.

Figure 2.

Potential products from the reaction of benzene with Pd/O₂/NO_x. Top (undesired) pathway: dimerization. Middle (undesired) pathway: nitration. Lower (desired) pathway: acetoxylation.

Figure 3.

A possible catalytic cycle for palladium-catalyzed, NO_x -mediated benzene C–H acetoxylation.

Figure 4. NO_x -bound organopalladium(IV) complexes synthesized by Campora. In the presence of O_2 , **3** converts to **4**.

Table 1

Pd-catalyzed aerobic oxidative coupling of benzene in acetic acid: Product ratios in the absence of a redox mediator.

$\text{PhH} \xrightarrow[\text{O}_2 \text{ (atm), AcOH}]{1\% \text{ or } 0.1\% \text{ Pd(OAc)}_2, 100^\circ\text{C, 10 h}} \text{PhOAc and PhOH} + \text{Ph-Ph}$ <div style="display: flex; justify-content: space-around; width: 100%;"> A B </div>				
Entry	%Pd ^a	O ₂ (atm) ^b	A:B (mmol)	TON ^c
1	1.0	1	1.0:1.0	0.4
2	0.1	1	1.7:1.0	1.1
3	0.1	10	1.6:1.0	0.8

^a 7 mmol scale; see SI for additional information.

^b "1 atm O₂" = 11 atm of 9% O₂ in N₂.

"10 atm O₂" = 111 atm of 9% O₂ in N₂.

^c Based on combined GC yields of PhOAc, PhOH, and Ph-Ph.

Table 2

$\text{Pd}(\text{OAc})_2/\text{NO}_x$ -catalyzed aerobic acetoxylation of benzene with low NO_x loading.

Entry	% Pd ^a	% NO _x	O ₂ (atm) ^b	TON (Pd) ^c	PhOAc:PhNO ₂ ^d
1	1.0	10% <i>t</i> -BuONO	1	4.0	10:1 ^e
2	0.1	1% <i>t</i> -BuONO	1	21	8.4:1
3	0.1	1% <i>t</i> -BuONO	10	26	27:1
4	0.1	1% <i>n</i> -pentylONO	10	25	25:1
5	0.1	1% NaNO ₃	10	23	26:1
6	0.1	1% fuming HNO ₃	10	15	22:1
7	0.05	0.5% <i>t</i> -BuONO	10	22	25:1
8	0.2	2% <i>t</i> -BuONO	10	21	11:1
9	0.1	0.5% <i>t</i> -BuONO	10	12	33:1

^a Entries 1 & 2 were conducted in sealed pressure tubes with teflon caps (1.75 mmol scale; 0.55 M). Entries 3–9 were conducted in Parr reactor vessels (7 mmol scale; 0.55 M). No PhOAc or PhNO_2 is observed in the absence of $\text{Pd}(\text{OAc})_2$.

^b For entries 3–9, “10 atm O₂” = 111 atm of 9% O₂ in N₂.

^c TONs were calculated based on calibrated GC yields of PhOAc.

^d Based on the ratio of calibrated GC yields.

^e Ratio of PhOAc:Ph-Ph (mmol) is 10:0.8. For all other entries, biphenyl is not observed.

Table 3Pd-catalyzed and NO_x-mediated aerobic acetoxylation of benzene: Optimization of turnover numbers.

Entry ^a	% NO _x	TON (Pd) ^b	PhOAc:PhNO ₂ ^c
1	30% <i>t</i> -BuONO	4	4:1
2	30% NaNO ₃	59	9:1
3	30% aq. HNO ₃ (70%)	115	25:1
4^d	30% fuming HNO₃	136	26:1
5	10% fuming HNO ₃	100	29:1
6	50% fuming HNO ₃	127	22:1
7	70% fuming HNO ₃	116	18:1
8	30% fuming HNO ₃ ; N ₂ (1 atm) instead of O ₂	19	1:1.2
9^e	30% fuming HNO₃, 85 °C, air (1 atm) instead of O₂	120	40:1

^a 1.2 mmol scale; 0.55 M. Reactions were conducted in sealed pressure tubes with teflon caps. Biphenyl is not observed.^b TONs were calculated based on calibrated GC yields of PhOAc.^c Based on the ratio of calibrated GC yields.^d Average of four experiments. Standard deviation for TON: 9.9. Standard deviation for ratio of PhOAc:PhNO₂: 3.3^e 13.56 mmol scale; 0.55 M. Reaction was conducted in a flask equipped with a reflux condenser. Biphenyl is not observed.