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The Aerobic Oxidation of Pd^{II} to Pd^{IV} by Active Radical Reactants: Direct C-H Nitration and Acylation of Arenes *via* Oxygenation Process with Molecular Oxygen

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ABSTRACT. A Pd-catalyzed aerobic oxidative C-H nitration and acylation of arenes with simple and readily available *tert*-butyl nitrite (TBN) and toluene as the radical precursors has been developed. Molecular oxygen is employed as the terminal oxidant and oxygen source to initiate the active radical reactants. Many different directing groups such as pyridine, pyrimidine, pyrazole, pyridol, pyridylketone, oxime, and azo groups, can be employed in these novel transformations. Pd^{II}/Pd^{IV} catalytic cycle through a radical process is the most likely pathway for these oxidative C-H nitration and acylation reactions.

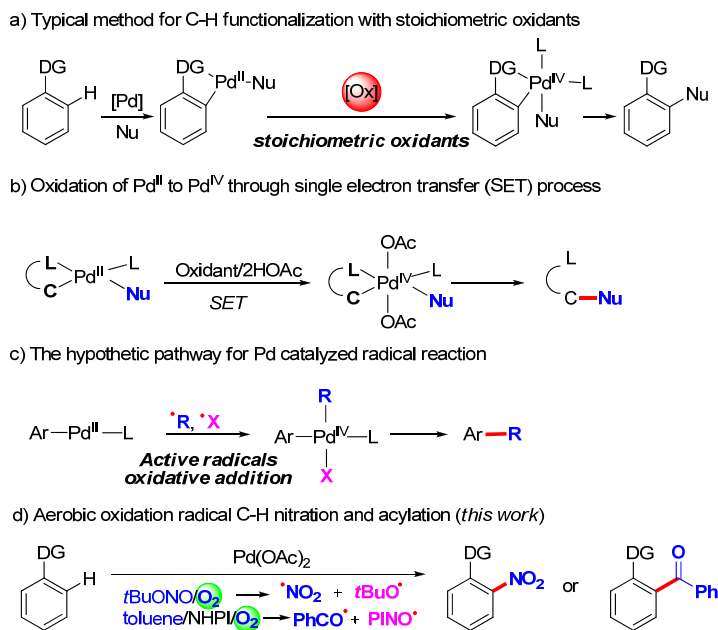
KEYWORDS. C-H functionalization, Oxygen, Nitration, Acylation, Palladium, Radicals, Regioselectivity.

INTRODUCTION:

Palladium-catalyzed C-H functionalization of organic substrates have been developed over the past decades as powerful and versatile tools in synthetic organic chemistry.¹⁻² Among them, the catalytic cycle between Pd^{II} and Pd^{IV} is one of the major pathway, in which a number of oxidants such as K₂S₂O₈, TBHP, BQ, DDQ, PIDA *etc.* have been widely employed (Scheme 1a). On behalf of the green and sustainable chemistry, molecular oxygen is considered as an ideal oxidant and offers attractive academic and industrial prospects.³⁻⁴ Therefore, the development of Pd-catalyzed oxidative C-H functionalization with molecular oxygen as oxidant is highly desirable. Although many protocols have been achieved on this topic under Pd/O₂ conditions, they were almost limited to oxidative Heck type reactions with Pd⁰/Pd^{II} catalytic cycle.⁴⁻⁵ It is well known that O₂ could oxidize Pd⁰ to Pd^{II} based on the standard electrode potential, but can hardly oxidize Pd^{II} to high-valent Pd species under ordinary conditions.⁶ Therefore, only a few examples that palladium-catalyzed aerobic oxidation formation of C-N,⁷ C-C,⁸ and C-O⁹ bond were reported through a reductive elimination process from high-valent Pd intermediates. Despite the significances of these reactions, the mechanism for the direct oxidation of Pd^{II} to high-valent Pd species is still unclear yet. More recently, Stahl^{7a} and Sanford^{9a} developed a significant palladium-catalyzed aerobic oxidative C-H functionalization, in which the Pd^{II} intermediates were probably oxidized to Pd^{IV} through single electron transfer (SET) process (Scheme 1b). Inspired by these reactions and our efforts on the aerobic oxidative C-H bond functionalization,¹⁰ we hypothesized that the active radical partner generated *in situ* could oxidize Pd^{II} to Pd^{IV}, and the subsequent reductive elimination may enable the C-H

functionalization with this radical precursor, providing new strategy for aryl C-H functionalization (Scheme 1c).

Scheme 1. Strategies for Palladium-catalyzed C-H Functionalization



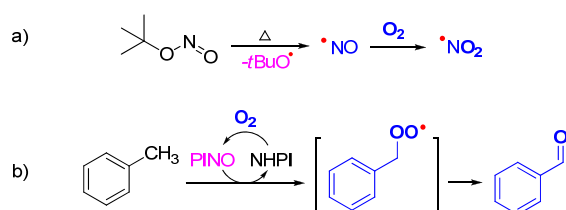
Herein, we report an efficient Pd(OAc)₂ catalyzed aerobic oxidative C-H nitration and acylation of arenes *via* a radical pathway (Scheme 1d). In this chemistry: 1) A radical process is reasonably involved in this aerobic catalytic cycle between Pd^{II} and Pd^{IV} species; 2) Simple and commercial available TBN and toluene are employed respectively as the radical precursors in these novel aerobic oxidative C-H nitration and acylation reactions. 3) Many kinds of directing groups (*e.g.* pyridine, pyrimidine, pyrazole, pyridol, pyridylketone, oxime, and azo groups) can be used in this direct transformation with broad substrate scope under mild conditions; 4) Environmentally benign molecular oxygen is employed as both oxidant and reagent.

RESULTS AND DISCUSSION:

According to this hypothesis, it is pre-requisite to find an aerobic oxidative pathway to generate active radicals, and will be very attractive to start from simple starting materials *via* dioxygen

activation,³⁻⁴ which would enable the direct oxygenation process using molecular oxygen as the oxygen source. It is known that the commercial available TBN can decompose into NO radical and *t*BuO radical by heating, and then the NO radical could be directly oxidized by O₂ to generate NO₂ radical (Scheme 2a).¹¹ On the other hand, on the basis of NHPI (*N*-hydroxyphthalimide) catalyzed aerobic oxygenation reactions,¹² we envisioned that PINO (phthalimido-*N*-oxyl) radical could be smoothly generated with molecular oxygen and the benzoyl radical can be produced from very simple toluene *via* single electron transfer (SET) processes (Scheme 2b). If the above proposed active N-radical and C-radical could be successfully generated in Pd^{II}-catalysis, the following relay of oxidation of Pd^{II}-intermediate to Pd^{IV} species and reductive elimination would occur to afford new C-N and C-C bond. In these cases, Pd-catalyzed *ortho* nitration and acylation of arenes with dioxygen as the terminal oxidant could be realized.

Scheme 2. (a) The Aerobic Oxidative Generation of *t*BuO Radical and NO₂ radical; (b) The Aerobic Oxidative Generation of PINO Radical and Benzoyl Radical.



Aromatic nitro compounds are important synthetic intermediates for the generation of pharmaceuticals, dyes, explosives, and materials.¹³ The classical electrophilic nitration of arenes¹⁴⁻¹⁵ is widely used for the synthesis of nitroarenes. Evidently, these methods suffer from some disadvantages of poor regioselectivity and limited functional group tolerance under harsh conditions such as strong acidic systems. In order to prepare nitroarenes at the specific position,

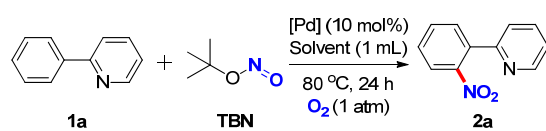
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6 transition-metal catalyzed coupling type nitration of aryl halides,¹⁶ aryl boronic acids¹⁷ and other
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8 prefunctionalized arenes¹⁸ have been developed. Alternatively, inspired by the development of
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10 directed C-H bond functionalization with a directing group, the synthesis of nitroarenes *via* direct
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12 C-H bond nitration has been an attractive topic.¹⁹ Despite the significances on the specific
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14 nitration position of these methodologies, the employment of expensive nitrite salts such as
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16 AgNO₂ as the nitro source and the additional stoichiometric oxidants such as peroxides,
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18 hypervalent iodine oxidants and toxic metal salts, limited their application.
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23 More recently, simple and readily available nitro source has been employed in the synthesis of
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25 nitroarenes.²⁰⁻²¹ Buchwald and coworkers developed an elegant protocol for the regioselective
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27 nitration of prefunctionalized aryl chlorides, triflates, and nonaflates with NaNO₂ as a simple
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29 nitro source.²⁰ Alternatively, Li *et al.* reported a significant Rh-catalyzed C-H nitration of arenes
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31 with NaNO₂ assisted by an expensive hypervalent iodine oxidant.^{21a} Therefore, although lots of
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33 nitration approaches have been developed in the past decades,¹⁶⁻²¹ it is still very attractive to
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35 develop better methodologies with: 1) environmentally benign oxidant, such as molecular
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37 oxygen; 2) broad scope of directing groups in the C-H bond nitration reaction.
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42 On the basis of the above hypothesis, we initiated our investigation by exploring the nitration
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44 of 2-phenylpyridine **1a** with simple, readily available TBN²² and O₂ as nitro source using
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46 Pd(OAc)₂ as catalyst. When the reaction was conducted in DCE at 80 °C, the *ortho*-nitration
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48 product **2a** was indeed isolated in 31% yield (entry 1, Table 1). Solvent screening showed that
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50 PhCl is a very suitable solvent for this transformation providing the product **2a** in 74% yield
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52 (entry 6). Whereas the reactions in other solvents such as CH₃CN, *t*Amyl-OH, CH₃NO₂ and
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54 toluene showed low efficiency (entries 2-5). The reaction catalyzed by PdCl₂ or PdTFA₂ gave
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56 lower yield than that catalyzed by Pd(OAc)₂ (entries 7-8). The reaction under air instead of pure
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molecular oxygen performed well but produced **2a** with a slightly lower yield (entry 9). However, the yield of **2a** declined dramatically when the reaction temperature decreased to 60 °C (entry 10). The reaction proceeded well in the dark, which indicated that the nitration is not initiated by photoirradiation (entry 11). As a control, no product **2a** was detected in the absence of Pd(OAc)₂ catalyst (entry 12). When NaNO₂, NaNO₃, and NO₂ gas were used respectively as nitro source instead of TBN, the nitration product was not obviously obtained (entries 13-14).

Table1. Optimization of the Reaction Conditions^a



entry	[Pd] (10 mol%)	solvent	yield (%) ^b
1	Pd(OAc) ₂	DCE	31
2	Pd(OAc) ₂	CH ₃ CN	26
3	Pd(OAc) ₂	<i>t</i> Amyl-OH	5
4	Pd(OAc) ₂	CH ₃ NO ₂	18
5	Pd(OAc) ₂	toluene	49
6	Pd(OAc)₂	PhCl	74
7	PdCl ₂	PhCl	40
8	PdTFA ₂	PhCl	70
9 ^c	Pd(OAc) ₂	PhCl	53
10 ^d	Pd(OAc) ₂	PhCl	10
11 ^e	Pd(OAc) ₂	PhCl	74
12	—	PhCl	0
13 ^f	Pd(OAc) ₂	PhCl	0
14 ^g	Pd(OAc) ₂	PhCl	trace

^aReaction conditions: **1a** (0.3 mmol), catalyst (10 mol%), TBN (2.0 equiv), solvent (1 mL), stirred at 80 °C under O₂ (1 atm) for 24 h. ^bIsolated yields. ^cThe reaction was carried out under air (1 atm). ^dThe reaction was carried out at 60 °C. ^eThe reaction was carried out in dark. ^fNaNO₃ or NaNO₂ was used as nitro source instead of TBN. ^gNO₂ gas was used as nitro source instead of TBN.

As shown in Table 2, a range of 2-arylpyridines underwent this *ortho*-nitration very well with TBN and dioxygen. It was found that either an electron-donating group, such as alkyl, alkoxy, phenyl, or electron-withdrawing group, such as halogen, trifluoromethyl, ethoxycarbonyl, nitro, at the 4-position (**2b-2j**), 2-position (**2k-2m**), or 3-position (**2n-2p**) of the phenyl ring was

compatible in this procedure leading to the corresponding nitration products in moderate to good yields. Consistent with previous Pd-catalyzed C-H functionalization studies,² the nitration of *meta*-substituted 2-arylpyridines occurred selectively at the less hindered position of the aromatic ring (**2n-2p**).

Table 2. Substrate Scope of Nitration of 2-Arylpyridines with TBN and Dioxygen^a

entry	product	yield	entry	product	yield
1	R = H	2a (74%)	17	R = 3-CH ₃	2q (79%)
2	R = CH ₃	2b (78%)	18	R = 4-CH ₃	2r (51%)
3	R = Ph	2c (63%)	19	R = 5-CH ₃	2s (73%)
4 ^b	R = OCH ₃	2d (66%)	20	R = 3,5-dimethyl	2t (74%)
5 ^b	R = OEt	2e (63%)			
6 ^b	R = Cl	2f (68%)	21		2u (72%)
7 ^b	R = F	2g (70%)			
8 ^b	R = CF ₃	2h (70%)	22		2v (50%)
9 ^b	R = COOCH ₃	2i (62%)			
10 ^b	R = NO ₂	2j (60%)			
11	R = CH ₃	2k (66%)			
12	R = OCH ₃	2l (55%)	23 ^b		2w (73%)
13 ^b	R = Cl	2m (55%)			
14	R = CH ₃	2n (62%)	24		2x (54%)
15	R = Cl	2o (76%)			
16 ^b	R = COOEt	2p (69%)			

^aStandard conditions: **1** (0.3 mmol), Pd(OAc)₂ (10 mol%), TBN (2.0 equiv), PhCl (1 mL), at 80 °C under O₂ (1 atm) for 24 h. Isolated yields. ^b3.0 equiv of TBN was employed at 100 °C.

It is noteworthy that pyrimidine and pyrazole rings were also effective directing groups in this transformation (**4a-4f**, Table 3). Moreover, phenyl(pyridin-2-yl)methanone was also tolerant to

provide the nitration product **4g** in moderate yield. Significantly, the sp^3 C-H bond of 8-methylquinoline reacted with 1.0 equiv of TBN and afforded benzyl nitro compound **4h** in moderate yield. Interestingly, the reaction conditions were equally applicable to 2-aryloxypyridine substrates (**4i-4q**).

Table 3. Substrate Scope of Nitration with TBN and Dioxygen Directed by Other Pyridine Groups^a

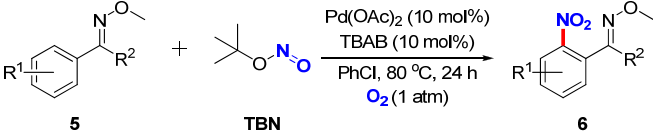
entry	product	yield	entry	product	yield
1	R = H	4a (79%)	9	R ¹ = H, R ² = H	4i (75%)
2	R = 2-CH ₃	4b (63%)	10	R ¹ = H, R ² = 4-CH ₃	4j (57%)
3	R = 3-OCH ₃	4c (58%)	11	R ¹ = H, R ² = 4-OCH ₃	4k (68%)
4	R = 3-CH ₃	4d (55%)	12	R ¹ = H, R ² = 4-I	4l (56%)
5		4e (78%)	13	R ¹ = H, R ² = 3-CH ₃	4m (57%)
6		4f (61%)	14	R ¹ = H, R ² = 2-CH ₃	4n (69%)
7		4g (69%)	15	R ¹ = 5-CH ₃ , R ² = H	4o (73%)
8 ^a		4h (56%)	16	R ¹ = 3-CH ₃ , R ² = H	4p (59%)
			17		4q (69%)

^aStandard conditions: **3** (0.3 mmol), Pd(OAc)₂ (10 mol%), TBN (3.0 equiv), PhCl (1 mL), at 100 °C under O₂ (1 atm) for 24 h. Isolated yields. ^b1.0 equiv of TBN was employed at 80 °C.

To investigate the scope of other directing groups in this C-H nitration reaction, we next examined several different arenes containing oxime groups (Table 4). When acetophenone *O*-methyl oxime **5a** was tested under the standard nitration conditions, *ortho*-nitrated product **6a** was isolated in 44% yield. The yield could be improved to 65% when 10 mol% of tetrabutyl

ammonium bromide (TBAB) was added as an additive into the reaction.²³ Acetophenoneoximes bearing both electron-donating (Me, OMe, *t*Bu) and electron-withdrawing (Br, F) substituents were successfully converted into the corresponding *ortho*-nitrated products (**6b-6g**). An *ortho*-methyl-substituted aryloxime was also tolerant in this transformation to afford the nitration product (**6h**). Additionally, when alkylphenone, benzaldehyde, and diarylketone *O*-methyl oximes were examined, the transformation still proceeded well to afford the desired products (**6i-6p**).

Table 4. C-H Bond Nitration with TBN and Dioxygen Directed by a Oxime Group^a

					
entry	product	yield	entry	product	yield
1		6a (65%)	10		6j (55%)
2		6b (58%)	11		6k (40%)
3		6c (44%)			
4		6d (61%)			
5 ^b		6e (48%)			
		6f (58%)	12		6l (71%)
6 ^b		6g (70%)	13		6m (53%)
7			14		6n (50%)
8 ^b		6h (47%)	15 ^b		6o (81%)
9		6i (64%)	16		6p (63%)

^aStandard conditions: **5** (0.3 mmol), Pd(OAc)₂ (10 mol%), TBAB (10 mol%), TBN (1.5 equiv), PhCl (1 mL) at 80 °C under O₂ (1 atm) for 24 h. Isolated yields. ^bThe reaction was carried out with 3.0 equiv of TBN at 100 °C.

The scope of the reaction with regard to azoarenes was then explored (Table 5).²⁴ The azoarenes with electron-donating groups proceeded faster than those with electron-withdrawing groups (**8a-8j**). When the reaction was performed with 3.0 equiv of TBN at 100 °C, the electron-deficient azoarenes can produce the desired products in moderate to excellent yields (**8d-8f**, **8h-8i**). Furthermore, we also examined the electronic effect of substituents on the regioselectivity of the *ortho*-nitration of unsymmetrical azoarenes. The results indicated that the *ortho*-nitration reactions occurred mainly on the electron-rich aryl rings (**8k-8l**).

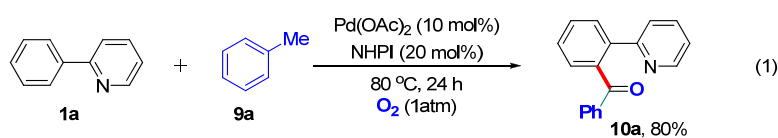
Table 5. C-H Bond Nitration with TBN and Dioxygen Directed by a Azo Group^a

entry	product	yield	entry	product	yield
1		8a (72%)	10		8j (80%)
2		8b (60%)			
3		8c (42%)	11		8k (64%)
4 ^b		8d (72%)			
5 ^b		8e (89%)	12		8l + 8l' , (75%) (1.5:1)
6 ^b		8f (82%)			
		8g (72%)			
7		8h (41%)			
8 ^b					
		8i (45%)			
9 ^b					

^aStandard conditions: **7** (0.3 mmol), Pd(OAc)₂ (10 mol%), TBAB (10 mol%), TBN (1.5 equiv), PhCl (1 mL) at 80 °C under O₂ (1 atm) for 24 h. Isolated yields. ^bThe reaction was carried out with 3.0 equiv of TBN at 100 °C.

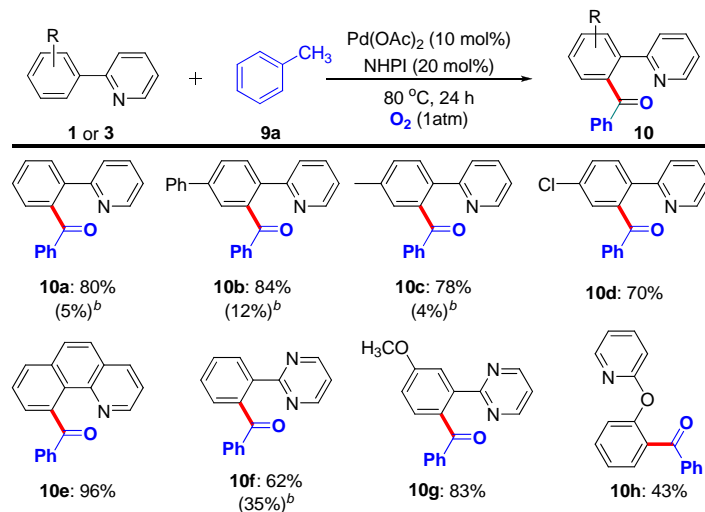
Hence, our hypothesis was proved reasonable by these positive results. Encouraged by this

successful radical nitration reaction, then we carried out the aerobic oxidative radical acylation project (Scheme 1d and Scheme 2b). As expected, under 1 atm of O₂, the reaction of **1a** with toluene (**9a**) as both the acylation reagent and solvent using 10 mol % Pd(OAc)₂ and 20 mol % NHPI as cocatalyst at 80 °C gave the acylation product aryl ketone (**10a**) in 80% yield with trace amount of dibenzoylated product formation (Eq. 1).²⁵ Aryl ketones are important structural units and synthetic precursors in natural products, pharmaceutical compounds, and functional materials.²⁶ The present acylation reaction provides a simple route for *ortho* acylation of arenes with molecular oxygen as the terminal oxidant and oxygen source to afford aryl ketones. Therefore, the aerobic oxidative nitration and acylation of arenes *via* dioxygen activation are successfully achieved through the proposed active radical oxidation strategy.



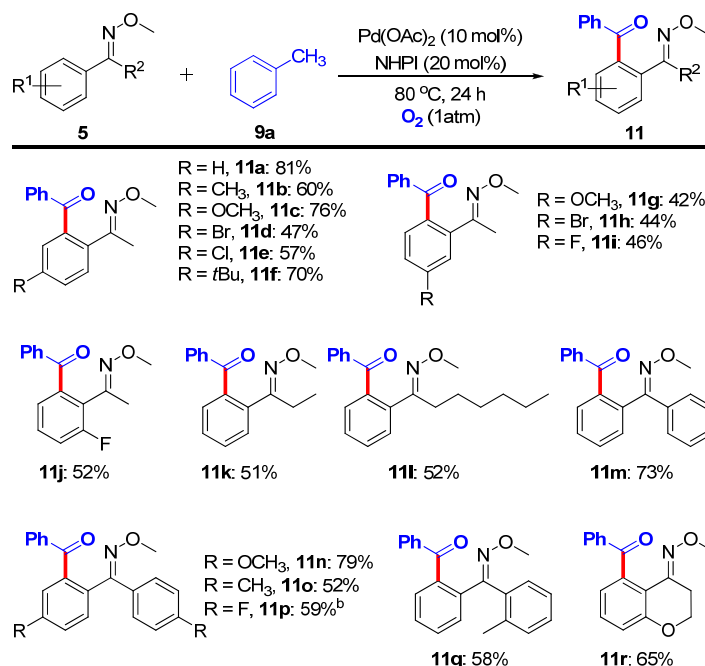
Followed these results, the acylation reaction by combination of toluene and molecular oxygen (Eq. 1) was also expanded to 2-arylpyridines and other arenes with different directing groups (Tables 6-8). For the 2-arylpyridines substrates (Table 6), the benzene rings with electron-donating and electron-withdrawing groups proceeded smoothly to give **10a-10d** in good to excellent yields. The reaction of benzo[*h*]quinoline and 2-arylpyrimidine were also examined and the excellent yields of products **10e-10g** were obtained. 2-Phenoxypyridine could be benzoylated to generate **10h** in moderate yield (Table 6).

Table 6. Acylation Reaction with Pyridine Groups^a



^aStandard conditions: **1** or **3** (0.5 mmol), $\text{Pd}(\text{OAc})_2$ (10 mol%), NHPI (20 mol%), toluene **9a** (1 mL) at 80 °C under O_2 (1 atm) for 24 h. Isolated yields. ^bIn some cases, diacylation occurred. The number in the parentheses is the yield of diacylation product.

Table 7. Acylation Reaction of *O*-methyl Oximes with Toluene^a



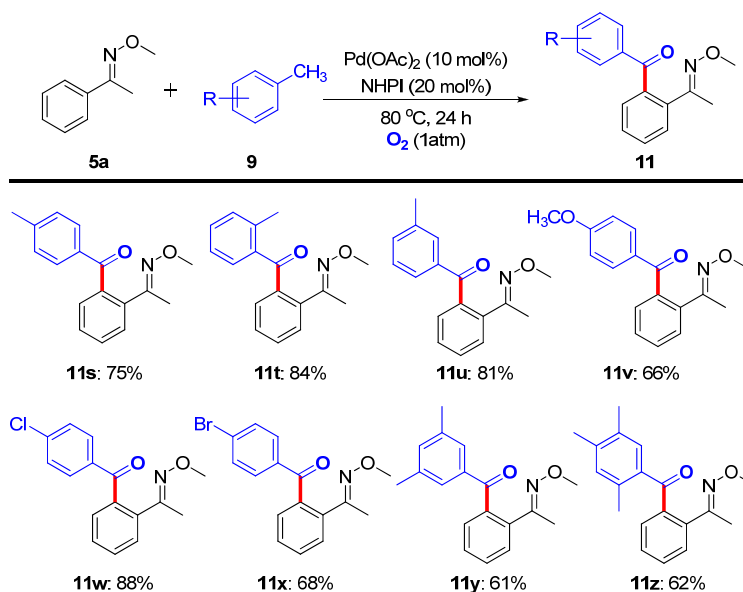
^aStandard conditions: **5** (0.5 mmol), $\text{Pd}(\text{OAc})_2$ (10 mol%), NHPI (20 mol%), toluene **9a** (1 mL) at 80 °C under O_2 (1 atm) for 24 h. Isolated yields. ^bAt 100 °C.

Subsequently, the acylation reaction of *O*-methyl oximes was investigated (Table 7). Under

the optimized acylation reaction conditions (See the Supporting Information), various substitutes at the *para*-position of the aryl ring were tolerated well to provide the products **11a-11f** in moderate to good yields. The electron-rich substrates generally provided superior efficiencies to electron-deficient substrates. The acylation of *meta*-substituted acetophenone *O*-methyl oximes were favored at the less hindered *ortho*-position, to produce the corresponding products **11g-11i**. An *ortho*-fluorine-substituted acetophenone *O*-methyl oxime gave the product in moderate yield (**11j**). Moreover, *O*-methyl oximes which derived from alkylphenone and diarylketone were also converted to the corresponding products (**11k-11q**). 4-Chromanone *O*-methyl oxime, with a bicyclic scaffold, reacted smoothly (**11r**). It is noted that the reaction of **5a** in 20 mmol scale afforded **11a** in 78% yield, which demonstrates the potential application in synthesis.

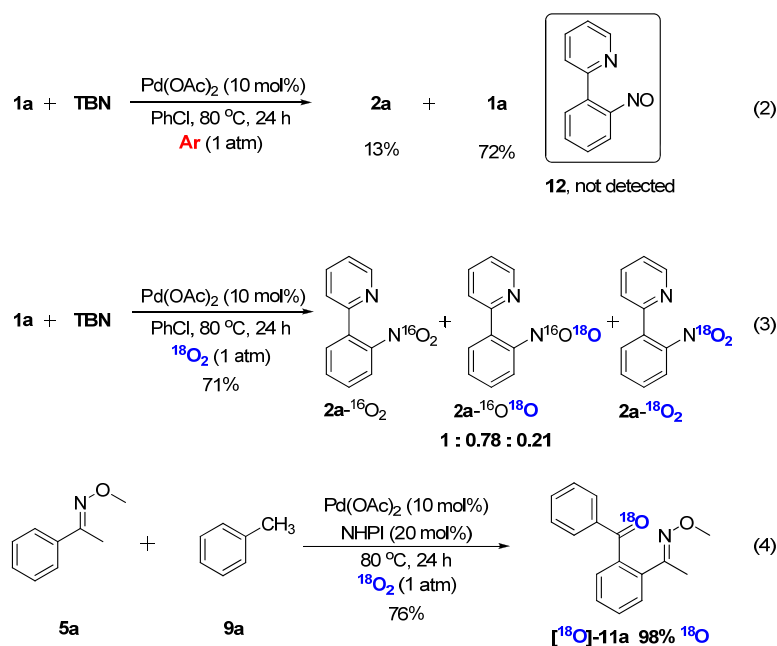
We next tested the scope of the toluene derivatives as the simple acyl source (Table 8). *p*-Xylene, *o*-xylene, *m*-xylene could reacted well to generate the products **11s-11u** in good yields. The reaction only occurred on one methyl group, with the other methyl group remaining intact. Electron-donating 4-methoxy-toluene gave slightly lower yield (**11v**). Furthermore, halo groups (Cl, Br) on aromatic rings were compatible (**11w-11x**), offering versatile synthetic functionality for further transformation. Multiple substituted toluenes smoothly executed this reaction with moderated yields (**11y-11z**).

Table 8. Scope of Toluene Derivatives as the Source of Acyl^a

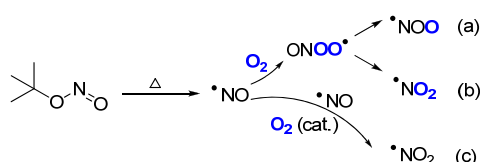


^aStandard conditions: **5a** (0.5 mmol), $\text{Pd}(\text{OAc})_2$ (10 mol%), NHPI (20 mol%), toluene derivatives **9** (1 mL) at $80\text{ }^\circ\text{C}$ under O_2 (1 atm) for 24 h. Isolated yields.

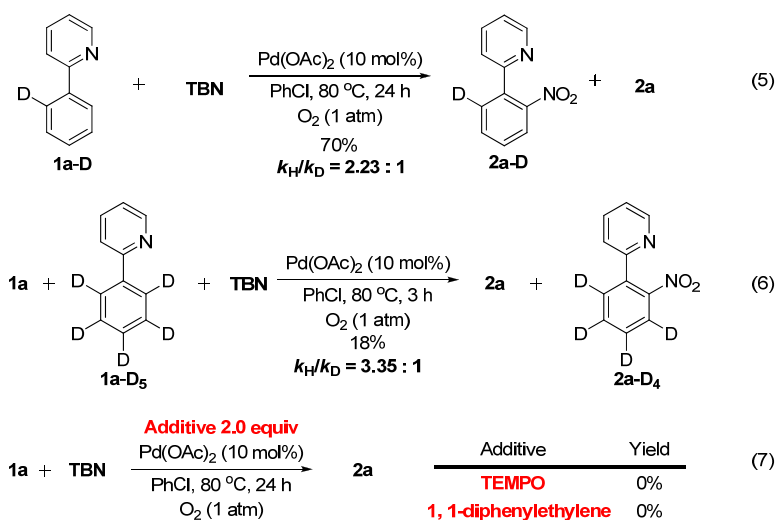
To obtain mechanistic insights into the present direct C-H nitration reaction, a series of experiments for mechanistic study were carried out. The reaction of **1a** under Ar atmosphere only produced **2a** in 13% yield with 72% of **1a** recovered (Eq. 2). The 2-(2-nitrosophenyl)pyridine **12** was not detected by GC-MS and *in situ* NMR in this reaction (Eq. 2), which illustrated that **12** is not the intermediate of this nitration. When the reaction was performed under $^{18}\text{O}_2$ atmosphere, three products were obtained (**2a**- $^{16}\text{O}_2$, **2a**- $^{18}\text{O}^{16}\text{O}$, **2a**- $^{18}\text{O}_2$, with the ratio of 1:0.78:0.21) (Eq. 3), which demonstrates that the NO_2 radical might be generated from NO radical through different processes under O_2 (Scheme 3). It is known that NO radical could be directly oxidized by O_2 to afford NO_2 radical (Scheme 3a and 3b) just as our design for this reaction (Scheme 2a).¹¹ Alternatively, the disproportionation reaction of NO radical catalyzed by O_2 occurs to give NO_2 radical (Scheme 3c).^{22i,27} Clearly, the oxygen atom of the generated carbonyl group originates from molecular oxygen in the aerobic acylation reaction proved by the ^{18}O -labeling experiment (Eq. 4).



Scheme 3. (a) and (b) The Generation of NO_2 Radical Through the Direct Oxidation of NO Radical with O_2 , (c) The Generation of NO_2 Radical Through the Disproportionation of NO Radical.

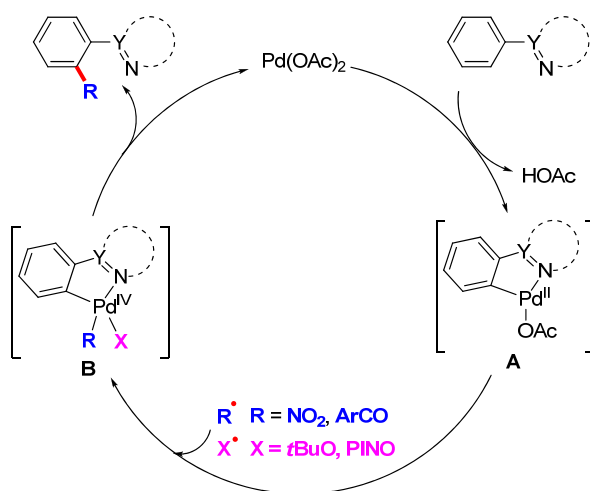


Furthermore, a kinetic isotopic effect (KIE) study was also conducted. The intramolecular $k_{\text{H}}/k_{\text{D}}$ of **1a** was determined to be 2.23 (Eq. 5) and the intermolecular $k_{\text{H}}/k_{\text{D}}$ was 3.35 (Eq. 6), which suggested that the C-H activation should be irreversible. Moreover, the reactions were completely inhibited in the presence of a radical scavenger such as TEMPO or 1,1-diphenylethylene (Eq. 7), which indicated that a radical process might be involved in this transformation.



On the basis of the above studies and reported literatures,^{7a,9a} a catalytic cycle of this Pd-catalyzed C-H nitration or acylation is illustrated in Scheme 4. The transformation occurs probably involving 1) the formation of palladacycle intermediate **A** by directing group assisted *ortho*-selective cyclometalation on the benzene ring of the substrate with Pd(OAc)₂; 2) oxidative addition of active radicals (NO₂ and *t*BuO radicals for nitration, ArCO and PINO radicals for acylation) to **A** provides Pd^{IV} intermediate²⁸⁻²⁹ **B**; 3) C-N or C-O bond formation through reductive elimination affords the corresponding products along with the regeneration of the Pd^{II} species.

Scheme 4. Proposed Mechanism



CONCLUSION :

In conclusion, we have developed Pd-catalyzed aerobic oxidative direct regioselective C-H nitration and acylation reactions with simple, inexpensive, and readily available *tert*-butyl nitrite (TBN) and toluene as the radical precursors. Molecular oxygen is employed as the terminal oxidant and oxygen source to initiate the active radical reactants. Many different directing groups such as pyridine, pyrimidine, pyrazole, pyridol, pyridylketone, oxime, and azo, can be employed in these novel C-H nitration and acylation transformations. The reaction proceeds under mild conditions and shows a broad substrate scope. These reactions may proceed *via* a Pd-mediated radical mechanism through the Pd^{II}/Pd^{IV} catalytic cycle. Further studies to elucidate the detailed reaction mechanism are ongoing in our group and we hope to disclose it in the near future.

ASSOCIATED CONTENT

Supporting Information. Experimental procedures, analytical data for products, NMR spectra of products. This material is available free of charge *via* the Internet at <http://pubs.acs.org>.

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Notes

The authors declare no competing financial interest.

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