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# Palladium-Catalyzed Aromatic C−H Bond Nitration Using Removable Directing Groups: Regiospecific Synthesis of Substituted *o*-Nitrophenols from Related Phenols

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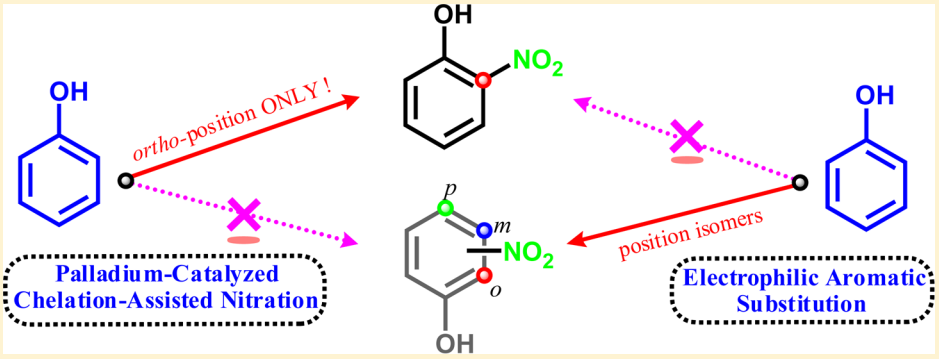
Supporting Information




**ABSTRACT:** A general and regiospecific transformation of substituted phenols into the related *o*-nitrophenols has been achieved via a three-step process involving the palladium-catalyzed chelation-assisted *ortho*-C−H bond nitration as the key step. In the process, 2-pyridinyloxy groups act as removable directing groups for the palladium-catalyzed *ortho*-nitration of substituted 2-phenoxypridines, and they can be readily removed in the subsequent conversion of the resulting 2-(2-nitrophenoxy)pyridines into 2-nitrophenols.

## INTRODUCTION

Nitroarenes are widely used as important raw materials in many disciplines of the chemical industry.[1] Besides, thanks to the versatile chemical transformations of the nitro group into other various functional groups, nitroarenes also serve as important platform molecules in organic synthesis.[2] To date, the most common and practical synthetic approach to nitroarenes is the direct electrophilic aromatic substitution with nitrating agents.[3] However, this nitration strategy has several persistent problems that are hard to overcome: (1) poor regioselectivity, especially for monosubstituted arenes, e.g., toluene, phenol, etc.; (2) poor chemoselectivity arising from over-nitrations (for example, the electrophilic nitrations of phenol sometimes give over-nitrated products as well besides mononitrated products);[4] (3) limited functional group and/or substrate compatibility due to the use of strongly acidic and oxidative reagents (e.g., mixed $H_2SO_4$ and $HNO_3$); and (4) difficult to achieve site-regiospecific nitration against the inherent orientation rules. For example, it is hard to realize regiospecific *ortho*-nitration of arenes substituted with *meta*-directing groups (e.g., aryl ketones, aldehydes, and acids etc.).

Inspired by the excellent regioselectivity achieved in the transition-metal-catalyzed chelation-assisted C−H bond functionalizations,[5] in 2010, we developed the first example of palladium-catalyzed *ortho*-specific nitration of aromatic C−H bonds by using *N*-heterocycles as directing groups.[6a] Since then, a similar chelation-directed strategy was explored in several palladium-,[6b,c,7,8] copper-,[9−12] and rhodium[13]-catalyzed *ortho*-nitrations of aryl $sp^2$ C−H bonds with various nitro sources by us and other groups. Compared with the traditional electrophilic nitration method, this new *ortho*-nitration protocol has several characteristic advantages: (1) excellent regioselectivity achieved by the $\sigma$-chelation-directed C−H cleavage; (2) excellent chemoselectivity to mononitrated products; and (3) broad functional group and substrate tolerance by using neutral or weak acidic reaction conditions. Despite promising progress, most of these reactions suffered from the use of *N*-heterocycles as the directing groups, which are difficult to be removed, thus adding a big drawback for the practical application in organic synthesis.

We envision that the introduction of removable and/or modifiable directing groups[14] for the C−H bond nitration could well circumvent the above-mentioned problem (Scheme 1). More importantly, by using such directing groups, we can expect that the nitro group could be regiospecifically introduced to the *ortho*-position of a target functional group even unnecessary to consider the effect of the inherent

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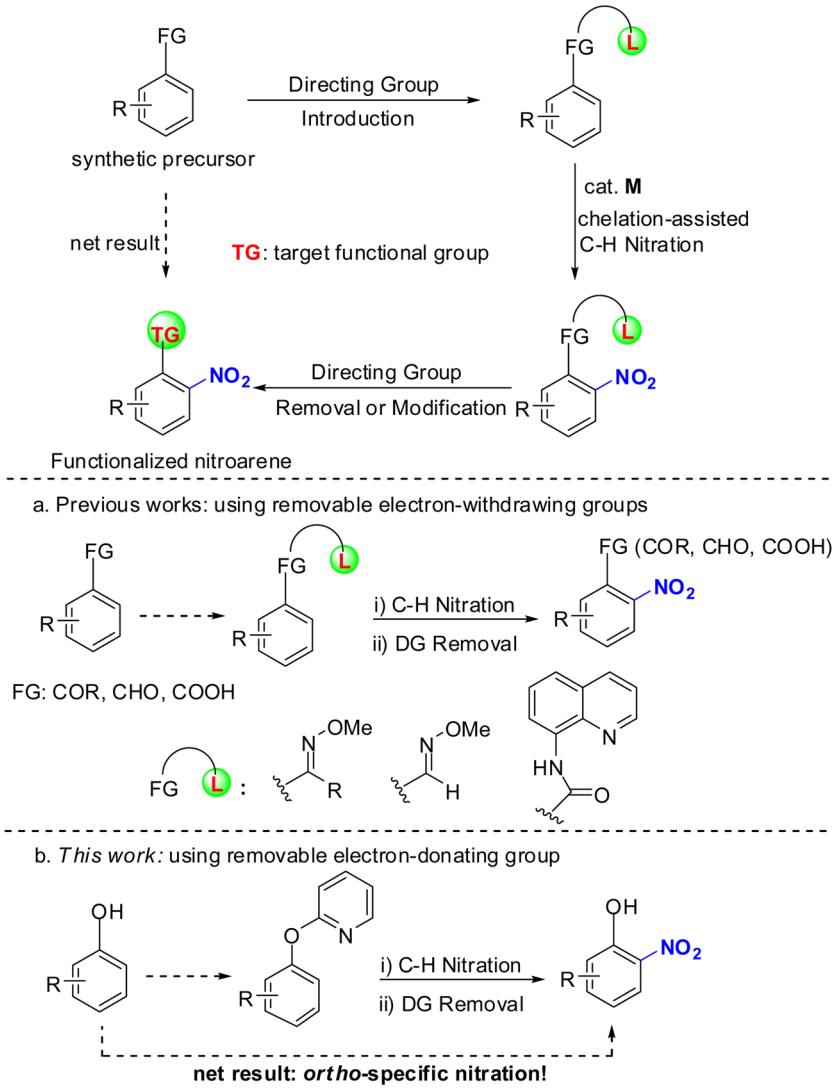
**Scheme 1. Strategy for the C−H Bond Nitration by Using Removable and/or Modifiable Directing Groups**




orientation rules[3] (Scheme 1)! For example, in our previous works,[6b,c] we realized the regiospecific synthesis of *o*-nitro aryl ketones and aldehydes by using electron-withdrawing *O*-methyl oximyl groups as the directing ligands. Very recently, the Gooßen group[12] reported the regiospecific synthesis of *o*-nitro aryl acids via a copper-mediated *ortho*-nitration of arenecarboxylates by using a Daugulis amide (also an electron-withdrawing group) as the removable directing groups. To the best of our knowledge, there is still no report on the use of removable electron-donating groups for the C−H bond nitration.[15] It is well known that pyridine directing groups (directing five-membered cyclopalladation) are usually difficult to be removed after C−H bond functionalizations. However, several research works disclosed that using benzyl pyridines,[16] 2-pyridinyloxy,[17] or oxazolines[18] to direct six- and/or seven-membered cyclopalladation may open up the possibility to remove the applied directing groups after C−H bond functionalizations. We herein present a palladium-catalyzed removable 2-pyridinyloxy group[17]-assisted C−H bond nitration, by which a general and regiospecific synthesis of substituted *o*-nitrophenols from the related phenols has been successfully developed (Scheme 1). It is well-known that *o*-nitrophenols[19] are a class of important intermediates in organic synthesis while their regiospecific nitration from phenols remains a hard task.[20]

## RESULTS AND DISCUSSION

Initially, 2-phenoxypyridine **1a**, readily prepared from the cross-coupling of phenol and 2-bromopyridine,[17c] was chosen as the model substrate to optimize the reaction conditions (Table 1). According to our previous works,[6a,b] the combination of $AgNO_2$ with $K_2S_2O_8$ can serve as an efficient nitro source for the palladium-catalyzed C−H bond nitration. Thus, under this combination, several palladium catalysts (10 mol % based on **1a**) were screened in DCE. It was found that $PdCl_2$ and $Pd(PPh_3)_2Cl_2$ showed low catalytic activity (entries 1 and 2, Table 1), whereas $Pd(OCOCF_3)_2$ exhibited better efficiency to give the desired product **2a** in 76% yield (entry 3, Table 1). When $Pd(OAc)_2$ was used, the reaction underwent very cleanly at 110 °C for 48 h and gave **2a** in a yield as high as 97% (entry 4, Table 1). Controlled experiments showed that the reaction failed to give the desired product in the absence of a palladium catalyst while the starting material was recovered (entry 5, Table 1). Several other nitro sources (e.g., $KNO_2$ and $NaNO_2$) as well as solvents (e.g., 1,4-dioxane and toluene) were surveyed for the reaction, and it was found that the reaction


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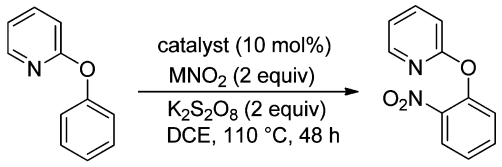
**Table 1. Optimization of Reaction Conditions**[a]




1a 2a

| entry | catalyst | $MNO_2$ | solvent | yield (%)[b] |
|---|---|---|---|---|
| 1 | $PdCl_2$ | $AgNO_2$ | DCE[c] | 44 |
| 2 | $Pd(PPh_3)_2Cl_2$ | $AgNO_2$ | DCE | 18 |
| 3 | $Pd(OCOCF_3)_2$ | $AgNO_2$ | DCE | 76 |
| **4** | **$Pd(OAc)_2$** | **$AgNO_2$** | **DCE** | **97(93[d])** |
| 5 | | $AgNO_2$ | DCE | 0 |
| 6 | $Pd(OAc)_2$ | $KNO_2$ | DCE | 10 |
| 7 | $Pd(OAc)_2$ | $NaNO_2$ | DCE | 36 |
| 8 | $Pd(OAc)_2$ | $AgNO_2$ | 1,4-dioxane | 21 |
| 9 | $Pd(OAc)_2$ | $AgNO_2$ | toluene | 17 |
| 10 | $Pd(OAc)_2$ | $AgNO_2$ | DCE | 23[e] |
| 11 | $Pd(OAc)_2$ | $AgNO_2$ | DCE | 58[f] |
| 12 | $Pd(OAc)_2$ | $AgNO_2$ | DCE | 87[g] |

[a]Reaction conditions: **1a** (0.3 mmol), catalyst (0.03 mmol), $AgNO_2$ (0.6 mmol), $K_2S_2O_8$ (0.6 mmol) in 3 mL of solvent at 110 °C for 48 h unless otherwise noted. [b]GC yields using phenanthrene as an internal standard. [c]DCE: 1,2-dichloroethane. [d]Isolated yields. [e]The reaction was conducted in the presence of 5 mol % of $Pd(OAc)_2$. [f]The reaction was performed on a 1 mmol scale of **1a** in the presence of 5 mol % of $Pd(OAc)_2$. [g]The reaction was performed on a 1 mmol scale of **1a** in the presence of 10 mol % of $Pd(OAc)_2$.

generally gave poor results under these conditions (entries 6−9, Table 1). The yield of **2a** was dramatically reduced when the catalyst loading decreased to 5 mol % (entry 10, Table 1). The nitration of **1a** on a scale of 1 mmol was also tried. In the presence of 5 and 10 mol % of $Pd(OAc)_2$, **2a** could be obtained in 58% and 87% yield, respectively (entries 11 and 12, Table 1).

Upon finishing the optimization of the reaction conditions, we turned our attention to investigate the scopes of the substrates. The results are summarized in Table 2. An investigation into a series of substituted 2-phenoxypyridines **1** showed that both electron-donating and electron-withdrawing groups on the phenyl ring were compatible under this procedure, and 2-(2-nitrophenoxy)pyridines **2** were isolated in moderate to excellent yields (39−95%, **2a**−**2w**, Table 2). The scope of the substituents was found to be broad, among which it includes halo (F, Cl, Br, and I), alkyl, aryl, methoxy, trifluoromethoxy, acetyl, and even acid-sensitive groups such as cyano and $-OCH_2O-$ groups. Note that the substituent pattern including *ortho*-, *meta*, and *para*-substituted ones has no much difference with regard to the yield and regioselectivity (e.g., **2d** vs **2g** vs **2p**, Table 2). When *meta*-substituted 2-phenoxypyridines having two regio-sites for nitration were used, the reaction exclusively gave one regioisomer in which the nitro group was introduced to the *para*-position to the already present substituent (**2e**−**g**, **2v**, Table 2). This exclusive regioselectivity might be ascribed to the steric effect upon the formation of the related palladacycle intermediate, where the cleavage of the less sterically hindered *o*-C−H bond is more favorable.[6b,21] When **1w** bearing a 5-chloro-2-pyridinyloxy group and **1x** bearing a 2-pyrimidinyloxy group were used, the reaction also underwent well to afford the desired product in 83% and 78% yield, respectively (**2w** and **2x**, Table 2). Apart from high regioselectivity, the present nitration procedure also exhibited excellent chemoselectivity; in all cases, only mononitrated products were obtained while over-nitrated products were not detected.

To fully demonstrate the synthetic potential of this methodology, the sequential removal of the 2-pyridinyloxy groups was tried. According to the reported literature,[17d] the 2-pyridinyloxy group could readily undergo depyridinylation via two steps: first, treatment with MeOTf in dry toluene at 100 °C for 2 h, then followed by refluxing in the Na/MeOH system for 15 min. Thus, through a three-step process consisting of DG introduction, C−H nitration, and DG removal, a general and regiospecific synthesis of *o*-nitrophenols from the related phenols has been successfully established for the first time. Several representative results for the preparation of *o*-nitrophenols **3** are listed in Table 3. A series of *o*-nitrophenols having different substituent patterns including *ortho*-, *meta*-, and *para*-substituted patterns could be regiospecifically synthesized in moderate to good yields (72−91%, Table 3). To our surprise, when **2g** was used, the depyridinylation could also give 4-bromo-2-methoxy nitrobenzene **3g′** in 62% yield apart from the desired **3g** (22% yield, Table 3). The depyridinylation of **2a** on a scale of 1 mmol was also carried out, and the reaction could successfully give the desired **3a** in 92% yield.

A series of mechanistic experiments were also conducted for a better understanding of the mechanism of the present C−H nitration (Schemes 2 and 3). First, the intermolecular competition experiment between an electron-deficient substrate **1o** and an electron-rich substrate **1h** was carried out under the standard reaction conditions for 24 h (eq 1, Scheme 2). It was found that the molar ratio of products **2o** and **2h** was 75:25. This result suggested that the C−H cleavage might involve in the concerted metalation deprotonation mechanism (CMD)[22] in which the cleavage of the C−H bond with enhanced acidity was more favorable. Next, the intermolecular KIE has also been measured on the basis of the competitive nitration between **1a** and **1a-$d_5$** (eq 2, Scheme 2). $^1H$ NMR analysis gave a $k_H/k_D$ = 2.0, suggesting that the cleavage of the C−H bond is the rate-determining step.

To further explore the catalytic species for the present C−H nitration, a binuclear palladacycle **A** was prepared from the stoichiometric reaction of **1a** with $Pd(OAc)_2$.[23] With employment of **A** as a catalyst, the nitration of the model substrate **1a** also underwent very well under otherwise identical to the standard conditions (eq 1, Scheme 3), implying that **A** might be a real catalyst. Finally, a suppression of C−H nitration was observed in the presence of the radical scavenger TEMPO (eq 2, Scheme 3), supporting that the reaction might involve a radical process.[24]

On the basis of the above mechanistic studies and previous reports,[6a,b,23,25−28] a plausible mechanism for the palladium-catalyzed *ortho*-nitration of 2-phenoxypyridine **1a** was proposed in Scheme 4. The reaction might start via the formation of the binuclear palladacycle species **A** from **1a** and $Pd(OAc)_2$.[23] Then, addition of $NO_2$ radicals[6a,b,25] to the metal center generated Pd(III)−Pd(III) species **B**[6a,b,26] and/or Pd(IV)−Pd(II) species **C**,[6a,b,27] which underwent reductive elimination through the $Pd^{II}/Pd^{III}$[26] and/or $Pd^{II}/Pd^{IV}$[27,28] catalytic cycles to afford **2a** and regenerate **A** in the presence of another molecule of **1a**.

## CONCLUSION

In summary, for the first time, we have successfully developed a general and regiospecific transformation of substituted phenols


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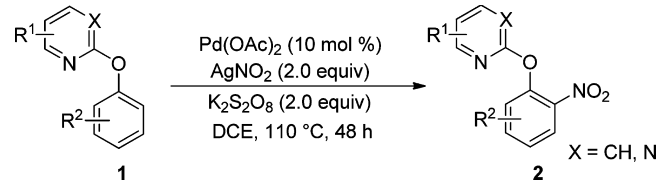
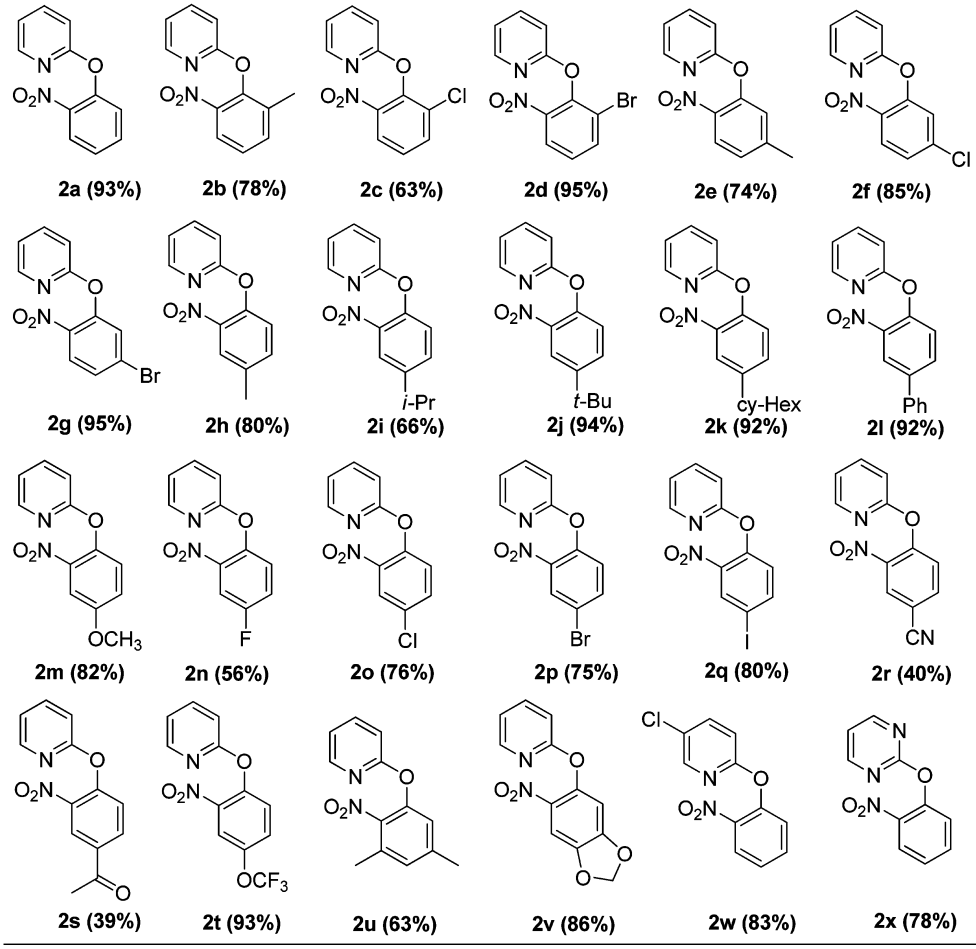
Table 2. Palladium-Catalyzed *Ortho*-Nitration of Substituted 2-Phenoxypyridines 1[a,b]




1 2




[a]Reaction conditions: **1** (0.3 mmol), $Pd(OAc)_2$ (0.03 mmol), $AgNO_2$ (0.6 mmol), $K_2S_2O_8$ (0.6 mmol) in 3.0 mL of DCE at 110 °C for 48 h. [b]Isolated yields.

to the corresponding *o*-nitrophenols via a three-step process consisting of the introduction of the 2-pyridinyloxy group, palladium-catalyzed C−H bond nitration, and the sequential removal of the directing group. The present protocol showed broad substrate and functional group tolerance and high regio- and chemoselectivity, which may provide an appealing approach for the synthesis of valuable *o*-nitrophenol derivatives.

## EXPERIMENTAL SECTION

**General Information.** Melting points are uncorrected. $^1H$ and $^{13}C$ NMR spectra were recorded on a spectrometer at 25 °C in $CDCl_3$ at 500 MHz and 125 MHz, respectively, with TMS as internal standard. Chemical shifts ($\delta$) are expressed in ppm, and coupling constants $J$ are given in Hz. The IR spectra were recorded on an FT-IR spectrometer. GC-MS experiments were performed with an EI source; high-resolution mass spectra (HRMS) were obtained on a TOF MS instrument with an EI or ESI source.

2-Phenoxypyridines (**1a**−**x**) were prepared according to the reported literature.[17c]

**General Procedure for the Synthesis of 2-(2-Nitrophenoxy)-pyridine 2 from 2-Phenoxypyridines 1.** A mixture of 2-phenoxypyridines **1** (0.30 mmol), $Pd(OAc)_2$ (6.7 mg, 0.03 mmol), $AgNO_2$ (92.3 mg, 0.6 mmol), $K_2S_2O_8$ (162.0 mg, 0.6 mmol), and anhydrous DCE (3.0 mL) was sealed in a 15 mL Schlenk flask. Then, the flask was stirred at 110 °C for 48 h. After being cooled to room temperature, the mixture was filtered with Celite and the filtrate was evaporated in vacuum; the residue was purified by flash column chromatography on silica gel with ethyl acetate/petroleum ether as the eluent to give pure **2**.

*2-(2-Nitrophenoxy)pyridine (**2a**).* Purified by column chromatography (petroleum ether/EtOAc, 6/1) as a white solid (60.3 mg, 93%); mp 57−58 °C; IR (KBr): $\nu$ = 1529 ($NO_2$) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz): $\delta$ 8.09−8.07 (m, 2H), 7.77−7.74 (m, 1H), 7.69−7.66 (m, 1H), 7.39−7.34 (m, 2H), 7.07 (d, $J$ = 8.5 Hz, 1H), 7.04−7.01 (m, 1H); $^{13}C$ NMR ($CDCl_3$, 125 MHz): $\delta$ 162.5, 147.1, 146.9, 142.7, 139.8, 134.4, 125.6, 125.34, 125.26, 119.1, 111.6; HRMS (ESI) for $C_{11}H_9N_2O_3$ $[M + H]^+$: calcd. 217.0613, found 217.0618.

*2-(2-Methyl-6-nitrophenoxy)pyridine (**2b**).* Purified by column chromatography (petroleum ether/EtOAc, 6/1) as a yellow oil (53.9 mg, 78%); IR (neat): $\nu$ = 1530 ($NO_2$) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500


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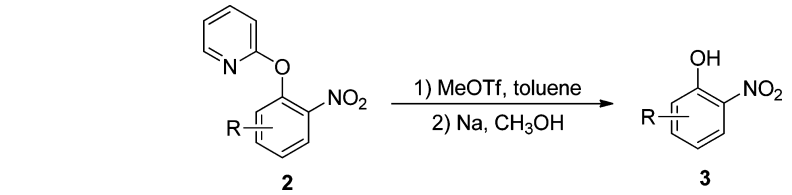
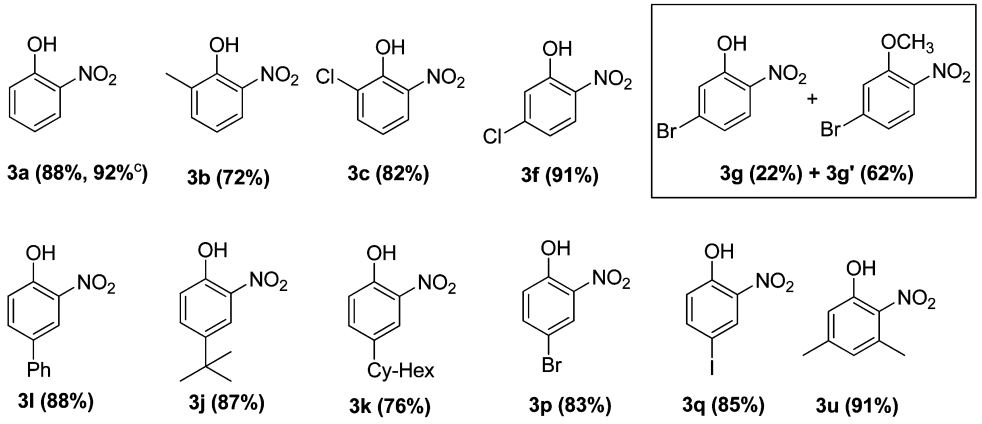
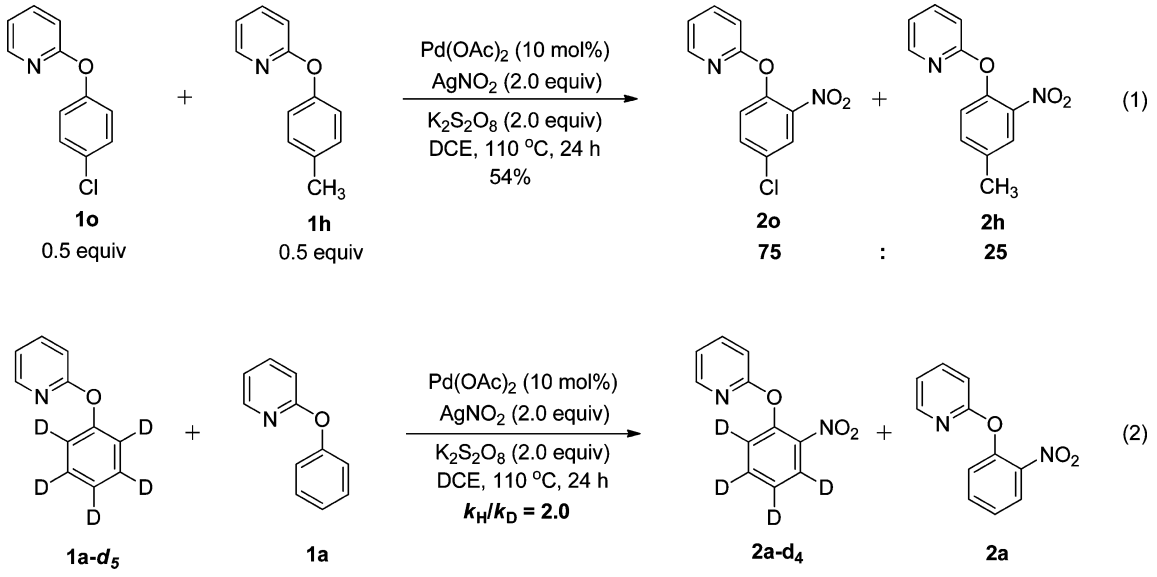
**Table 3. Synthesis of *o*-Nitrophenols 3 through Depyridinylation of 2-(2-Nitrophenoxy)pyridines 2[a,b,c]**




[a]Reaction conditions: (i) **2** (0.2 mmol), MeOTf (1.8 equiv) in dry toluene at 100 °C for 2 h. (ii) Na (24 equiv), $CH_3OH$ (10 mL), reflux, 15 min. [b]Isolated yields. [c]The reaction was performed on a scale of 1 mmol of **2a**.

**Scheme 2. Studies on the Intermolecular Competition Experiments**




MHz): $\delta$ 8.05 (dd, $J_1$ = 5.0 Hz, $J_2$ = 1.5 Hz, 1H), 7.90 (dd, $J_1$ = 8.0 Hz, $J_2$ = 1.0 Hz, 1H), 7.77–7.73 (m, 1H), 7.56 (dd, $J_1$ = 8.0 Hz, $J_2$ = 1.0 Hz, 1H), 7.30 (d, $J$ = 8.0 Hz, 1H), 7.07 (d, $J$ = 8.5 Hz, 1H), 7.01–6.99 (m, 1H), 2.27 (s, 3H); $^{13}$C NMR ($CDCl_3$, 125 MHz): $\delta$ 162.4, 147.2, 145.0, 143.5, 139.8, 135.9, 135.1, 125.2, 123.3, 118.7, 110.9, 16.7; HRMS (ESI) for $C_{12}H_{11}N_2O_3$ [M + H]$^+$: calcd. 231.0770, found 231.0778.

*2-(2-Chloro-6-nitrophenoxy)pyridine (**2c**).* Purified by column chromatography (petroleum ether/EtOAc, 6/1) as a white solid (47.4 mg, 63%); mp 100–101 °C; IR (KBr): $\nu$ = 1530 ($NO_2$) cm$^{-1}$; $^1$H NMR ($CDCl_3$, 500 MHz): $\delta$ 8.04 (dd, $J_1$ = 5.0 Hz, $J_2$ = 1.5 Hz, 1H), 7.99 (dd, $J_1$ = 8.0 Hz, $J_2$ = 1.5 Hz, 1H), 7.78–7.76 (m, 2H), 7.36 (t, $J$ = 8.5 Hz, 1H), 7.14 (d, $J$ = 8.5 Hz, 1H), 7.06–7.03 (m, 1H); $^{13}$C NMR ($CDCl_3$, 125 MHz): $\delta$ 161.8, 147.0, 144.6, 143.7, 139.9, 135.1, 131.2, 125.8, 124.0, 119.2, 111.0; HRMS (ESI) for $C_{11}H_8ClN_2O_3$ [M + H]$^+$: calcd. 251.0223, found 251.0216.

*2-(2-Bromo-6-nitrophenoxy)pyridine (**2d**).* Purified by column chromatography (petroleum ether/EtOAc, 6/1) as a white solid (84.1 mg, 95%); mp 103–104 °C; IR (KBr): $\nu$ = 1530 ($NO_2$) cm$^{-1}$; $^1$H NMR ($CDCl_3$, 500 MHz): $\delta$ 8.05–8.03 (m, 2H), 7.93 (dd, $J_1$ = 8.0 Hz, $J_2$ = 1.5 Hz, 1H), 7.80–7.76 (m, 1H), 7.30 (t, $J$ = 8.0 Hz, 1H), 7.13 (d, $J$ = 8.5 Hz, 1H), 7.05–7.03 (m, 1H); $^{13}$C NMR ($CDCl_3$, 125 MHz): $\delta$ 161.8, 147.1, 144.8, 139.9, 138.1, 133.7, 126.3, 124.7, 120.6, 119.2, 111.2; HRMS (ESI) for $C_{11}H_8BrN_2O_3$ [M + H]$^+$: calcd. 294.9718, found 294.9710.

*2-(5-Methyl-2-nitrophenoxy)pyridine (**2e**).* Purified by column chromatography (petroleum ether/EtOAc, 6/1) as a yellow oil (51.1 mg, 74%); IR (neat): $\nu$ = 1521 ($NO_2$) cm$^{-1}$; $^1$H NMR ($CDCl_3$, 500 MHz): $\delta$ 8.07 (dd, $J_1$ = 5.0 Hz, $J_2$ = 1.5 Hz, 1H), 8.02 (d, $J$ = 8.5 Hz,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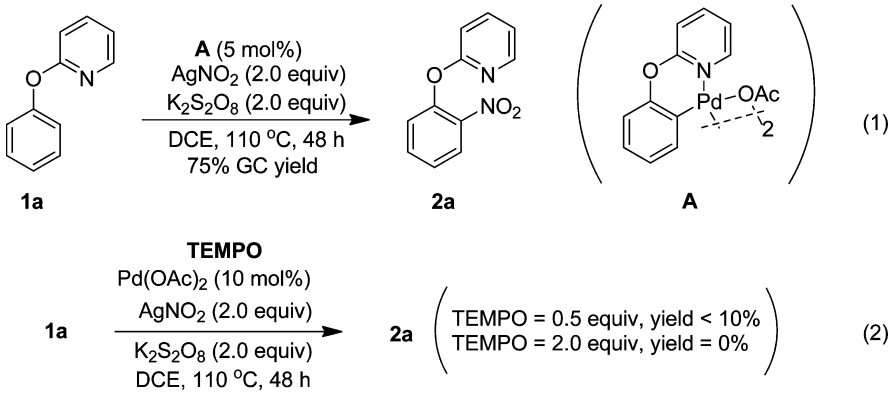
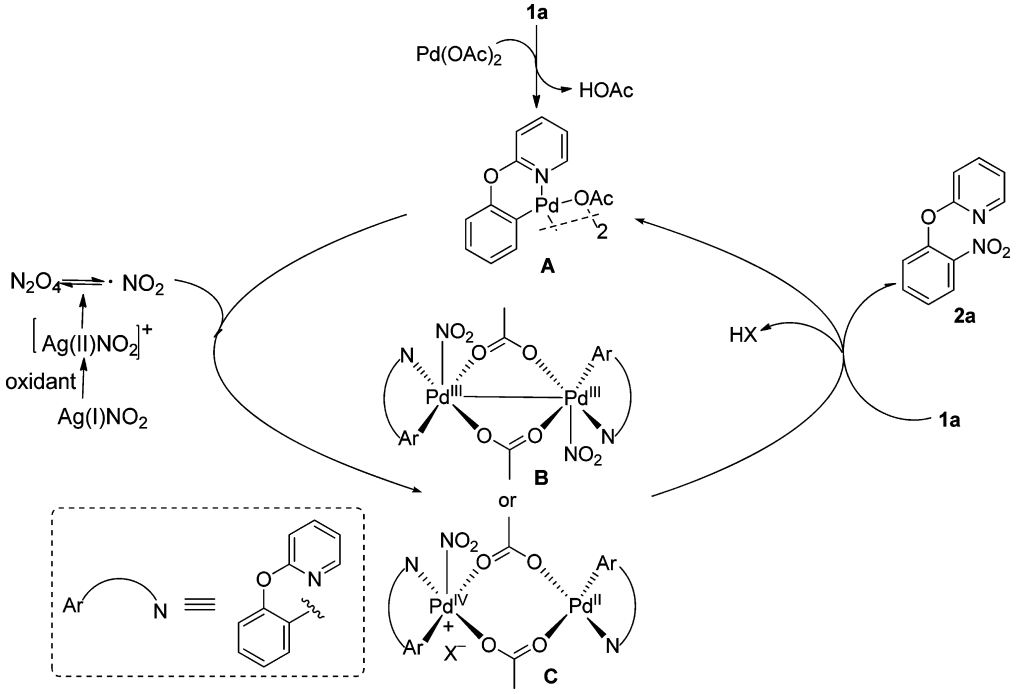
**Scheme 3. Studies on the Catalytic Species and the Effect of Radical Scavenger TEMPO**




**Scheme 4. Proposed Mechanism**




1H), 7.76−7.73 (m, 1H), 7.16 (d, $J$ = 8.5 Hz, 1H), 7.14 (s, 1H), 7.06 (d, $J$ = 8.5 Hz, 1H), 7.03−7.01 (m, 1H), 2.46 (s, 3H); $^{13}$C NMR ($CDCl_3$, 125 MHz): $\delta$ 162.7, 147.2, 146.9, 146.4, 140.3, 139.7, 126.2, 125.8, 125.6, 119.0, 111.6, 21.6; HRMS (ESI) for $C_{12}H_{11}N_2O_3$ $[M + H]^+$: calcd. 231.0770, found 231.0765.

*2-(5-Chloro-2-nitrophenoxy)pyridine (**2f**).* Purified by column chromatography (petroleum ether/EtOAc, 6/1) as a white solid (63.9 mg, 85%); mp 76−77 °C; IR (KBr): $\nu$ = 1525 ($NO_2$) $cm^{-1}$; $^1$H NMR ($CDCl_3$, 500 MHz): $\delta$ 8.08−8.04 (m, 2H), 7.76 (dd, $J_1$ = 8.5 Hz, $J_2$ = 1.5 Hz, 1H), 7.37−7.33 (m, 2H), 7.09−7.04 (m, 2H); $^{13}$C NMR ($CDCl_3$, 125 MHz): $\delta$ 162.0, 147.7, 147.1, 141.2, 140.3, 140.0, 126.7, 125.60, 125.57, 119.5, 111.6; HRMS (ESI) for $C_{11}H_8ClN_2O_3$ $[M + H]^+$: calcd. 251.0223, found 251.0229.

*2-(5-Bromo-2-nitrophenoxy)pyridine (**2g**).* Purified by column chromatography (petroleum ether/EtOAc, 6/1) as a white solid (84.1 mg, 95%); mp 95−96 °C; IR (KBr): $\nu$ = 1522 ($NO_2$) $cm^{-1}$; $^1$H NMR ($CDCl_3$, 500 MHz): $\delta$ 8.07 (dd, $J_1$ = 5.0 Hz, $J_2$ = 1.5 Hz, 1H), 7.97 (d, $J$ = 9.0 Hz, 1H), 7.79−7.75 (m, 1H), 7.54−7.50 (m, 2H), 7.09−7.04 (m, 2H); $^{13}$C NMR ($CDCl_3$, 125 MHz): $\delta$ 162.0, 147.5, 147.1, 140.0, 128.6, 128.5, 128.4, 126.7, 119.5, 111.6; HRMS (ESI) for $C_{11}H_8BrN_2O_3$ $[M + H]^+$: calcd. 294.9718, found 294.9726.

*2-(4-Methyl-2-nitrophenoxy)pyridine (**2h**).* Purified by column chromatography (petroleum ether/EtOAc, 6/1) as a yellow oil (55.5 mg, 80%); IR (neat): $\nu$ = 1532 ($NO_2$) $cm^{-1}$; $^1$H NMR ($CDCl_3$, 500 MHz): $\delta$ 8.07 (d, $J$ = 3.5 Hz, 1H), 7.90 (s, 1H), 7.76−7.72 (m, 1H), 7.47 (dd, $J_1$ = 8.5 Hz, $J_2$ = 1.5 Hz, 1H), 7.23 (d, $J$ = 8.5 Hz, 1H), 7.07−7.00 (m, 2H), 2.46 (s, 3H); $^{13}$C NMR ($CDCl_3$, 125 MHz): $\delta$ 162.7, 147.1, 144.6, 139.7, 135.8, 129.6, 125.8, 125.1, 118.9, 111.5, 20.7; HRMS (ESI) for $C_{12}H_{11}N_2O_3$ $[M + H]^+$: calcd. 231.0770, found 231.0777.

*2-(4-Isopropyl-2-nitrophenoxy)pyridine (**2i**).* Purified by column chromatography (petroleum ether/EtOAc, 6/1) as a yellow oil (51.1 mg, 66%); IR (neat): $\nu$ = 1532 ($NO_2$) $cm^{-1}$; $^1$H NMR ($CDCl_3$, 500 MHz): $\delta$ 8.08 (dd, $J_1$ = 5.0 Hz, $J_2$ = 2.0 Hz, 1H), 7.93 (s, 1H), 7.76−7.73 (m, 1H), 7.53 (dd, $J_1$ = 8.5 Hz, $J_2$ = 2.0 Hz, 1H), 7.26 (d, $J$ = 8.5 Hz, 1H), 7.07−7.00 (m, 2H), 3.06−3.00 (m, 1H), 1.33 (d, $J$ = 6.5 Hz, 6H); $^{13}$C NMR ($CDCl_3$, 125 MHz): $\delta$ 162.7, 147.1, 146.5, 144.7, 142.4, 139.7, 132.7, 125.0, 123.4, 118.9, 111.5, 33.5, 29.7, 23.7; HRMS (ESI) for $C_{14}H_{15}N_2O_3$ $[M + H]^+$: calcd. 259.1083, found 259.1075.

*2-(4-tert-Butyl-2-nitrophenoxy)pyridine (**2j**).* Purified by column chromatography (petroleum ether/EtOAc, 6/1) as a white solid (76.8 mg, 94%); mp 66−67 °C; IR (KBr): $\nu$ = 1533 ($NO_2$) $cm^{-1}$; $^1$H NMR ($CDCl_3$, 500 MHz): $\delta$ 8.0 8 (dd, $J_1$ = 5.0 Hz, $J_2$ = 1.5 Hz, 1H), 8.06 (d, $J$ = 2.0 Hz, 1H), 7.76−7.72 (m, 1H), 7.68 (dd, $J_1$ = 8.5 Hz, $J_2$ = 2.5 Hz, 1H), 7.26 (s, 1H), 7.06 (d, $J$ = 8.0 Hz, 1H), 7.01 (dd, $J_1$ = 7.0 Hz, $J_2$ = 5.0 Hz, 1H), 1.39 (s, 9H); $^{13}$C NMR ($CDCl_3$, 125 MHz): $\delta$ 162.6,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149.0, 147.1, 144.5, 142.1, 139.7, 131.7, 124.7, 122.5, 118.9, 111.6, 34.8, 31.2; HRMS (ESI) for $C_{15}H_{17}N_2O_3$ $[M + H]^+$: calcd. 273.1239, found 273.1234.

*2-(4-Cyclohexyl-2-nitrophenoxy)pyridine* (**2k**). Purified by column chromatography (petroleum ether/EtOAc, 6/1) as a white solid (82.3 mg, 92%); mp 88−89 °C; IR (KBr): $\nu$ = 1531 ($NO_2$) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz): $\delta$ 8.08 (dd, $J_1$ = 5.0 Hz, $J_2$ = 1.5 Hz, 1H), 7.91 (d, $J$ = 2.0 Hz, 1H), 7.76−7.73 (m, 1H), 7.51 (dd, $J_1$ = 8.0 Hz, $J_2$ = 2.0 Hz, 1H), 7.25 (d, $J$ = 8.5 Hz, 1H), 7.06−7.00 (m, 2H), 2.64−2.59 (m, 1H), 1.96−1.88 (m 4H), 1.47−1.27 (m, 6H); $^{13}C$ NMR ($CDCl_3$, 125 MHz): $\delta$ 162.7, 147.1, 145.8, 144.7, 142.4, 139.8, 133.1, 125.0, 123.7, 118.9, 111.6, 43.7, 34.2, 26.7, 25.9; HRMS (ESI) for $C_{17}H_{19}N_2O_3$ $[M + H]^+$: calcd. 299.1396, found 299.1389.

*2-((3-Nitro-[1,1′-biphenyl]-4-yl)oxy)pyridine* (**2l**). Purified by column chromatography (petroleum ether/EtOAc, 6/1) as a white solid (80.7 mg, 92%); mp 83−84 °C; IR (KBr): $\nu$ = 1533 ($NO_2$) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz): $\delta$ 8.29 (d, $J$ = 2.0 Hz, 1H), 8.11 (dd, $J_1$ = 5.0 Hz, $J_2$ = 1.5 Hz, 1H), 7.88 (dd, $J_1$ = 8.5 Hz, $J_2$ = 2.0 Hz, 1H), 7.79−7.76 (m, 1H), 7.64−7.62 (m, 2H), 7.52−7.49 (m, 2H), 7.45−7.42 (m, 2H), 7.11 (d, $J$ = 8.0 Hz, 1H), 7.06−7.04 (m, 1H); $^{13}C$ NMR ($CDCl_3$, 125 MHz): $\delta$ 162.5, 147.1, 146.0, 142.8, 139.9, 139.0, 138.3, 132.8, 129.1, 128.3, 127.0, 125.6, 124.0, 119.2, 111.6; HRMS (ESI) for $C_{17}H_{12}N_2O_3$ $[M + H]^+$: calcd. 293.0926, found 293.0933.

*2-(4-Methoxy-2-nitrophenoxy)pyridine* (**2m**). Purified by column chromatography (petroleum ether/EtOAc, 6/1) as a white solid (60.6 mg, 82%); mp 79−80 °C; IR (KBr): $\nu$ = 1532 ($NO_2$) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz): $\delta$ 8.07−8.06 (m, 1H), 7.75−7.72 (m, 1H), 7.59 (d, $J$ = 3.0 Hz, 1H), 7.26−7.21 (m, 2H), 7.06−6.99 (m, 2H), 3.90 (s, 3H); $^{13}C$ NMR ($CDCl_3$, 125 MHz): $\delta$ 162.9, 156.6, 147.1, 142.8, 140.3, 139.7, 126.4, 121.2, 118.8, 111.4, 109.7, 56.1; HRMS (ESI) for $C_{12}H_{11}N_2O_4$ $[M + H]^+$: calcd. 247.0719, found 247.0715.

*2-(4-Fluoro-2-nitrophenoxy)pyridine* (**2n**). Purified by column chromatography (petroleum ether/EtOAc, 6/1) as a white solid (39.3 mg, 56%); mp 85−86 °C; IR (KBr): $\nu$ = 1537 ($NO_2$) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz): $\delta$ 8.05 (dd, $J_1$ = 5.0, Hz, $J_2$ = 1.5 Hz, 1H), 7.82 (dd, $J_1$ = 7.5 Hz, $J_2$ = 3.0 Hz, 1H), 7.78−7.75 (m, 1H), 7.43−7.39 (m, 1H), 7.35 (dd, $J_1$ = 5.0 Hz, $J_2$ = 4.0 Hz, 1H), 7.09−7.02 (m, 2H); $^{13}C$ NMR ($CDCl_3$, 125 MHz): $\delta$ 162.4, ?, 147.0, ?, 139.9, 127.0 (d, $J_{F-C}$ = 8.8 Hz), 121.6 (d, $J_{F-C}$ = 23.8 Hz), 119.2, ?, 112.9 ($J_{F-C}$ = 22.5 Hz), 111.4; HRMS (ESI) for $C_{11}H_8FN_2O_3$ $[M + H]^+$: calcd. 235.0519, found 235.0527.

*2-(4-Chloro-2-nitrophenoxy)pyridine* (**2o**). Purified by column chromatography (petroleum ether/EtOAc, 6/1) as a white solid (57.1 mg, 76%); mp 102−103 °C; IR (KBr): $\nu$ = 1532 ($NO_2$) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz): $\delta$ 8.08 (d, $J$ = 2.5 Hz, 1H), 8.06 (dd, $J_1$ = 5.0, Hz, $J_2$ = 1.5 Hz, 1H), 7.79−7.75 (m, 1H), 7.63 (t, $J$ = 8.5 Hz, 1H), 7.32 (d, $J$ = 8.0 Hz, 1H), 7.09−7.03 (m, 2H); $^{13}C$ NMR ($CDCl_3$, 125 MHz): $\delta$ 162.2, 147.1, 145.6, 142.9, 134.0, 134.4, 130.7, 126.7, 125.7, 119.4, 111.6; HRMS (ESI) for $C_{11}H_8ClN_2O_3$ $[M + H]^+$: calcd. 251.0223, found 251.0218.

*2-(4-Bromo-2-nitrophenoxy)pyridine* (**2p**). Purified by column chromatography (petroleum ether/EtOAc, 6/1) as a white solid (66.4 mg, 75%); mp 94−95 °C; IR (KBr): $\nu$ = 1532 ($NO_2$) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz): $\delta$ 8.22 (d, $J$ = 2.5 Hz, 1H), 8.06 (dd, $J_1$ = 5.0 Hz, $J_2$ = 1.5 Hz, 1H), 7.78−7.75 (m, 2H), 7.26 (d, $J$ = 8.0 Hz, 1H), 7.09−7.04 (m, 2H); $^{13}C$ NMR ($CDCl_3$, 125 MHz): $\delta$ 162.1, 147.1, 146.0, 140.0, 137.3, 132.2, 128.5, 126.9, 119.4, 117.7, 111.6; HRMS (ESI) for $C_{11}H_8BrN_2O_3$ $[M + H]^+$: calcd. 294.9718, found 294.9713.

*2-(4-Iodo-2-nitrophenoxy)pyridine* (**2q**). Purified by column chromatography (petroleum ether/EtOAc, 6/1) as a white solid (82.1 mg, 80%); mp 101−102 °C; IR (KBr): $\nu$ = 1528 ($NO_2$) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz): $\delta$ 8.36 (d, $J$ = 2.0 Hz, 1H), 8.06 (dd, $J_1$ = 5.0 Hz, $J_2$ = 1.5 Hz, 1H), 7.95 (dd, $J_1$ = 8.5 Hz, $J_2$ = 2.0 Hz, 1H), 7.78−7.74 (m, 1H), 7.12−7.03 (m, 3H); $^{13}C$ NMR ($CDCl_3$, 125 MHz): $\delta$ 162.2, 147.1, 146.9, 143.3, 143.2, 139.9, 134.2, 127.1, 119.4, 111.7, 87.3; HRMS (ESI) for $C_{11}H_8IN_2O_3$ $[M + H]^+$: calcd. 342.9580, found 342.9589.

*3-Nitro-4-(pyridin-2-yloxy)benzonitrile* (**2r**). Purified by column chromatography (petroleum ether/EtOAc, 6/1) as a white solid (28.9 mg, 40%); mp 143−144 °C; IR (KBr): $\nu$ = 1533 ($NO_2$) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz): $\delta$ 8.36 (d, $J$ = 2.0 Hz, 1H), 8.07 (dd, $J_1$ = 5.0 Hz, $J_2$ = 1.5 Hz, 1H), 7.92 (dd, $J_1$ = 8.5 Hz, $J_2$ = 2.0 Hz, 1H), 7.83−7.80 (m, 1H), 7.51 (d, $J$ = 8.5 Hz, 1H), 7.14−7.10 (m, 2H); $^{13}C$ NMR ($CDCl_3$, 125 MHz): $\delta$ 161.4, 150.5, 147.1, 142.7, 140.3, 137.3, 129.7, 126.2, 120.2, 116.4, 112.0, 109.2; HRMS (ESI) for $C_{12}H_8N_3O_3$ $[M + H]^+$: calcd. 242.0566, found 242.0558.

*1-(3-Nitro-4-(pyridin-2-yloxy)phenyl)ethanone* (**2s**). Purified by column chromatography (petroleum ether/EtOAc, 6/1) as a white solid (30.2 mg, 39%); mp 55−56 °C; IR (KBr): $\nu$ = 1530 ($NO_2$) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz): $\delta$ 8.63 (d, $J$ = 2.5 Hz, 1H), 8.25 (dd, $J_1$ = 8.0 Hz, $J_2$ = 2.0 Hz, 1H), 8.08 (dd, $J_1$ = 5.0 Hz, $J_2$ = 2.0 Hz, 1H), 7.81−7.78 (m, 1H), 7.45 (d, $J$ = 8.5 Hz, 1H), 7.13 7.07 (m, 3H), 2.68 (s, 3H); $^{13}C$ NMR ($CDCl_3$, 125 MHz): $\delta$ 194.8, 161.9, 150.5, 147.2, 142.4, 140.1, 134.0, 133.7, 126.0, 125.3, 119.8, 111.9, 26.5; HRMS (ESI) for $C_{13}H_{11}N_2O_4$ $[M + H]^+$: calcd. 259.0719, found 259.0725.

*2-(2-Nitro-4-(trifluoromethoxy)phenoxy)pyridine* (**2t**). Purified by column chromatography (petroleum ether/EtOAc, 6/1) as a white solid (83.8 mg, 93%); mp 48−49 °C; IR (KBr): $\nu$ = 1540 ($NO_2$) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz): $\delta$ 8.07 (dd, $J_1$ = 5.0 Hz, $J_2$ = 1.5 Hz, 1H), 7.96 (d, $J$ = 2.5 Hz, 1H), 7.79−7.76 (m, 1H), 7.55 (dd, $J_1$ = 9.0 Hz, $J_2$ = 2.5 Hz, 1H), 7.41 (d, $J$ = 9.0 Hz, 1H), 7.10−7.06 (m, 2H); $^{13}C$ NMR ($CDCl_3$, 125 MHz): $\delta$ 162.1, 147.0, 145.3, 145.19, 142.7, 140.0, 126.9, 126.8, 120.0 (q, $J_{F-C}$ = 257.0 Hz), 119.5, 118.5, 111.6; HRMS (ESI) for $C_{12}H_8F_3N_2O_4$ $[M + H]^+$: calcd. 301.0436, found 301.0442.

*2-(3,5-Dimethyl-2-nitrophenoxy)pyridine* (**2u**). Purified by column chromatography (petroleum ether/EtOAc, 6/1) as a white solid (46.2 mg, 63%); mp 75−76 °C; IR (KBr): $\nu$ = 1528 ($NO_2$) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz): $\delta$ 8.17 (dd, $J_1$ = 5.0 Hz, $J_2$ = 1.5 Hz, 1H), 7.74−7.70 (m, 1H), 7.05−7.03 (m, 1H), 6.98 (d, $J$ = 8.0 Hz, 1H), 6.95 (d, $J$ = 7.5 Hz, 2H), 2.38 (s, 3H), 2.37 (s, 3H); $^{13}C$ NMR ($CDCl_3$, 125 MHz): $\delta$ 162.7, 147.4, 145.5, 142.7, 141.8, 139.7, 131.7, 128.1, 121.7, 119.2, 111.7, 21.4, 17.7; HRMS (ESI) for $C_{13}H_{13}N_2O_3$ $[M + H]^+$: calcd. 245.0926, found 245.0931.

*2-((6-Nitrobenzo[d][1,3]dioxol-5-yl)oxy)pyridine* (**2v**). Purified by column chromatography (petroleum ether/EtOAc, 6/1) as a white solid (67.1 mg, 86%); mp 107−108 °C; IR (KBr): $\nu$ = 1527 ($NO_2$) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz): $\delta$ 8.08 (dd, $J_1$ = 5.0 Hz, $J_2$ = 1.5 Hz, 1H), 7.77−7.73 (m, 1H), 7.61 (s, 1H), 7.06 (d, $J$ = 8.0 Hz, 1H), 7.03−7.01 (m, 1H), 6.77 (s, 1H), 6.15 (s, 2H); $^{13}C$ NMR ($CDCl_3$, 125 MHz): $\delta$ 162.8, 152.6, 147.1, 144.9, 144.4, 139.8, 136.3, 119.0, 111.5, 105.7, 105.3, 103.3; HRMS (ESI) for $C_{12}H_9N_2O_5$ $[M + H]^+$: calcd. 261.0511, found 261.0517.

*5-Chloro-2-(2-nitrophenoxy)pyridine* (**2w**). Purified by column chromatography (petroleum ether/EtOAc, 6/1) as a white solid (62.3 mg, 83%); mp 82−83 °C; IR (KBr): $\nu$ = 1530 ($NO_2$) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz): $\delta$ 8.10 (dd, $J_1$ = 8.0 Hz, $J_2$ = 1.5 Hz, 1H), 8.00 (d, $J$ = 2.5 Hz, 1H), 7.72−7.67 (m, 2H), 7.42−7.33 (m, 2H), 7.04 (d, $J$ = 8.5 Hz, 1H); $^{13}C$ NMR ($CDCl_3$, 125 MHz): $\delta$ 160.9, 150.1, 146.6, 145.5, 142.6, 139.7, 134.6, 126.6, 125.8, 125.3, 112.5; HRMS (ESI) for $C_{11}H_8ClN_2O_3$ $[M + H]^+$: calcd. 251.0223, found 251.0227.

*2-(2-Nitrophenoxy)pyrimidine* (**2x**). Purified by column chromatography (petroleum ether/EtOAc, 6/1) as a white solid (50.8 mg, 78%); mp 115−116 °C; IR (KBr): $\nu$ = 1529 ($NO_2$) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz): $\delta$ 8.54 (d, $J$ = 5.0 Hz, 1H), 8.15 (dd, $J_1$ = 8.0 Hz, $J_2$ = 1.5 Hz, 1H), 7.74−7.70 (m, 1H), 7.45−7.39 (m, 2H), 7.09 (t, $J$ = 5.0 Hz, 1H); $^{13}C$ NMR ($CDCl_3$, 125 MHz): $\delta$ 164.3, 159.7, 146.0, 142.1, 135.0, 126.3, 125.9, 125.3, 116.8; HRMS (ESI) for $C_{10}H_8N_3O_3$ $[M + H]^+$: calcd. 218.0566, found 218.0559.

**General Procedure for the Synthesis of *o*-Nitrophenols 3 through Depyridinylation of Compound 2.** Under an argon atmosphere, to a well-stirred solution of **2** (0.2 mmol) in dry toluene (5 mL) was added MeOTf (39.8 $\mu$L, 0.36 mmol) at 100 °C for 2 h. After cooling to room temperature, the solution was evaporated under vacuum. Without purification, the crude product was subsequently added into a Na (110.4 mg, 4.8 mmol)/MeOH (5 mL) solution, heated to reflux, and stirred for a further 15 min. After cooling to room temperature, the solvent was evaporated under vacuum and water (15 mL) was added to the residue. The aqueous solution was extracted by


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ethyl acetate (10 mL × 3), and the organic layers were combined, dried over MgSO4, filtered, and evaporated under vacuum. The residue was further purified by silica gel chromatography using petroleum/ethyl acetate (6/1, V/V) as the eluent to give pure **3**.

*2-Nitrophenol (**3a**).*[29] Purified by column chromatography (petroleum ether/EtOAc, 6/1) as a yellow solid (22.4 mg, 88%); mp 45−46 °C (lit.[29] mp 46−47 °C); IR (KBr): $\nu$ = 3350 (OH), 1518 ($NO_2$) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz): $\delta$ 10.60 (s, 1H), 8.12 (dd, $J_1$ = 8.5 Hz, $J_2$ = 1.5 Hz, 1H), 7.62−7.58 (m, 1H), 7.17 (dd, $J_1$ = 8.5 Hz, $J_2$ = 1.5 Hz, 1H), 7.02−6.99 (m, 1H); $^{13}C$ NMR ($CDCl_3$, 125 MHz): $\delta$ 155.1, 137.5, 133.7, 125.1, 120.2, 120.0; MS (EI, 70 ev): $m/z$ (%) = 139 [$M^+$].

*2-Methyl-6-nitrophenol (**3b**).*[30] Purified by column chromatography (petroleum ether/EtOAc, 6/1) as a yellow solid (22.0 mg, 72%); mp 72−73 °C (lit.[30] mp 71−73 °C); IR (KBr): $\nu$ = 3250 (OH), 1521 ($NO_2$) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz): $\delta$ 10.93 (s, 1H), 7.97 (d, $J$ = 8.5 Hz, 1H), 7.46 (d, $J$ = 7.0 Hz, 1H), 6.90 (dd, $J_1$ = 8.5 Hz, $J_2$ = 2.5 Hz, 1H), 2.35 (s, 3H); $^{13}C$ NMR ($CDCl_3$, 125 MHz): $\delta$ 153.7, 138.1, 133.5, 129.5, 122.6, 119.3, 15.8; MS (EI, 70 ev): $m/z$ (%) = 153 [$M^+$].

*2-Chloro-6-nitrophenol (**3c**).*[30] Purified by column chromatography (petroleum ether/EtOAc, 6/1) as a yellow solid (28.5 mg, 82%); mp 68−69 °C (lit.[30] mp 70−71 °C); IR (KBr): $\nu$ = 3294 (OH), 1521 ($NO_2$) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz): $\delta$ 11.06 (s, 1H), 8.08 (dd, $J_1$ = 9.0 Hz, $J_2$ = 1.5 Hz, 1H), 7.72 (dd, $J_1$ = 7.5 Hz, $J_2$ = 1.5 Hz, 1H), 6.98 (t, $J$ = 8.5 Hz, 1H); $^{13}C$ NMR ($CDCl_3$, 125 MHz): $\delta$ 151.5, 137.6, 134.6, 124.7, 123.7, 119.7; MS (EI, 70 ev): $m/z$ (%) = 173 [$M^+$].

*5-Chloro-2-nitrophenol (**3f**).*[31] Purified by column chromatography (petroleum ether/EtOAc, 6/1) as a yellow solid (31.6 mg, 91%); mp 42−43 °C (lit.[31] mp 42−43 °C); IR (KBr): $\nu$ = 3436 (OH), 1529 ($NO_2$) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz): $\delta$ 10.67 (s, 1H), 8.08 (d, $J$ = 9.0 Hz, 1H), 7.20 (d, $J$ = 2.5 Hz, 1H), 6.99 (dd, $J_1$ = 9.0 Hz, $J_2$ = 2.0 Hz, 1H); $^{13}C$ NMR ($CDCl_3$, 125 MHz): $\delta$ 155.5, 143.8, 132.4, 126.2, 121.0, 119.9; MS (EI, 70 ev): $m/z$ (%) = 173 [$M^+$].

*5-Bromo-2-nitrophenol (**3g**).*[31] Purified by column chromatography (petroleum ether/EtOAc, 6/1) as a white solid (9.5 mg, 22%); mp 47−48 °C (lit.[31] mp 46−47 °C); IR (KBr): $\nu$ = 3436 (OH), 1528 ($NO_2$) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz): $\delta$ 10.63 (s, 1H), 7.99 (d, $J$ = 9.0 Hz, 1H), 7.39 (d, $J$ = 2.0 Hz, 1H), 7.15 (dd, $J_1$ = 9.0 Hz, $J_2$ = 2.0 Hz, 1H); $^{13}C$ NMR ($CDCl_3$, 125 MHz): $\delta$ 155.4, 143.8, 132.4, 126.1, 123.9, 123.1; MS (EI, 70 ev): $m/z$ (%) = 217 [$M^+$].

*4-Bromo-2-methoxy-1-nitrobenzene (**3g′**).*[32] Purified by column chromatography (petroleum ether/EtOAc, 6/1) as a white solid (28.8 mg, 62%); mp 91−92 °C (lit.[32] mp 91−92 °C); IR (KBr): $\nu$ = 1521 ($NO_2$) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz): $\delta$ 7.77 (d, $J$ = 8.5 Hz, 1H), 7.26 (d, $J$ = 2.0 Hz, 1H), 7.20 (dd, $J_1$ = 8.5 Hz, $J_2$ = 2.0 Hz, 1H), 3.99 (s, 3H); $^{13}C$ NMR ($CDCl_3$, 125 MHz): $\delta$ 153.6, 137.6, 128.5, 126.9, 123.6, 117.3, 56.9; MS (EI, 70 ev): $m/z$ (%) = 231 [$M^+$].

*3-Nitro-[1,1′-biphenyl]-4-ol (**3l**).*[33] Purified by column chromatography (petroleum ether/EtOAc, 6/1) as a white solid (37.9 mg, 88%); mp 68−69 °C (lit.[33] mp 68−69 °C); IR (KBr): $\nu$ = 3437 (OH), 1536 ($NO_2$) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz): $\delta$ 10.60 (s, 1H), 8.32 (d, $J$ = 2.0 Hz, 1H), 7.84 (dd, $J_1$ = 8.5 Hz, $J_2$ = 2.0 Hz, 1H), 7.56 (d, $J$ = 7.5 Hz, 2H), 7.48 (t, $J$ = 7.5 Hz, 2H), 7.41 (t, $J$ = 7.5 Hz, 1H), 7.25 (d, $J$ = 9.0 Hz, 1H); $^{13}C$ NMR ($CDCl_3$, 125 MHz): $\delta$ 154.3, 138.2, 136.3, 133.84, 133.77, 129.1, 128.0, 126.7, 122.8, 120.4; MS (EI, 70 ev): $m/z$ (%) = 215 [$M^+$].

*4-(tert-Butyl)-2-nitrophenol (**3j**).*[30] Purified by column chromatography (petroleum ether/EtOAc, 6/1) as a white solid (34.0 mg, 87%); mp 68−70 °C (lit.[30] mp 70−73 °C); IR (KBr): $\nu$ = 3298 (OH), 1524 ($NO_2$) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz): $\delta$ 10.48 (s, 1H), 8.08 (d, $J$ = 2.5 Hz, 1H), 7.65 (dd, $J_1$ = 9.0 Hz, $J_2$ = 2.5 Hz, 1H), 7.11 (d, $J$ = 9.0 Hz, 1H), 1.34 (s, 9H); $^{13}C$ NMR ($CDCl_3$, 125 MHz): $\delta$ 153.1, 143.7, 135.5, 133.1, 120.9, 119.5, 34.4, 31.1; MS (EI, 70 ev): $m/z$ (%) = 195 [$M^+$].

*4-Cyclohexyl-2-nitrophenol (**3k**).*[34] Purified by column chromatography (petroleum ether/EtOAc, 6/1) as a yellow oil (33.6 mg, 76%); IR (neat): $\nu$ = 3249 (OH), 1536 ($NO_2$) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz): $\delta$ 10.47 (s, 1H), 7.93 (d, $J$ = 2.0 Hz, 1H), 7.46 (dd, $J_1$ = 8.5 Hz, $J_2$ = 2.5 Hz, 1H), 7.09 (d, $J$ = 8.5 Hz, 1H), 2.54−2.49 (m, 1H), 1.89−1.86 (m, 4H), 1.42−1.25 (m, 6H); $^{13}C$ NMR ($CDCl_3$, 125 MHz): $\delta$ 153.3, 140.5, 136.8, 133.4, 122.2, 119.7, 43.3, 34.2, 26.6, 25.9; MS (EI, 70 ev): $m/z$ (%) = 221 [$M^+$].

*4-Bromo-2-nitrophenol (**3p**).*[35] Purified by column chromatography (petroleum ether/EtOAc, 6/1) as a white solid (36.2 mg, 83%); mp 89−90 °C (lit.[35] mp 89−92 °C); IR (KBr): $\nu$ = 3249 (OH), 1536 ($NO_2$) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz): $\delta$ 10.51 (s, 1H), 8.26 (d, $J$ = 2.5 Hz, 1H), 7.68 (dd, $J_1$ = 9.0 Hz, $J_2$ = 2.5 Hz, 1H), 7.09 (d, $J$ = 9.0 Hz, 1H); $^{13}C$ NMR ($CDCl_3$, 125 MHz): $\delta$ 154.1, 140.4, 134.1, 127.3, 121.7, 111.7; MS (EI, 70 ev): $m/z$ (%) = 217 [$M^+$].

*4-Iodo-2-nitrophenol (**3q**).*[36] Purified by column chromatography (petroleum ether/EtOAc, 6/1) as a white solid (45.1 mg, 85%); mp 81−82 °C (lit.[36] mp 81 °C); IR (KBr): $\nu$ = 3294 (OH), 1521 ($NO_2$) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz): $\delta$ 10.53 (s, 1H), 8.43 (d, $J$ = 2.5 Hz, 1H), 7.84 (dd, $J_1$ = 8.5 Hz, $J_2$ = 2.0 Hz, 1H), 6.97 (d, $J$ = 9.0 Hz, 1H); $^{13}C$ NMR ($CDCl_3$, 125 MHz): $\delta$ 154.8, 145.9, 134.5, 133.3, 122.0, 80.4; MS (EI, 70 ev): $m/z$ (%) = 265 [$M^+$].

*3,5-Dimethyl-2-nitrophenol (**3u**).*[37] Purified by column chromatography (petroleum ether/EtOAc, 6/1) as a white solid (30.5 mg, 91%); mp 66−67 °C (lit.[37] mp 64−65.5 °C); IR (KBr): $\nu$ = 3436 (OH), 1527 ($NO_2$) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz): $\delta$ 10.63 (s, 1H), 6.82 (s, 1H), 6.65 (s, 1H), 2.61 (s, 3H), 2.33 (s, 3H); $^{13}C$ NMR ($CDCl_3$, 125 MHz): $\delta$ 155.8, 147.2, 136.8, 133.2, 125.3, 117.6, 22.6, 21.6; MS (EI, 70 ev): $m/z$ (%) = 167 [$M^+$].

**Mechanistic Studies.** *Intermolecular Competition Experiment on **1o** and **1h**.* A mixture of **1o** (0.15 mmol), **1h** (0.15 mmol), $Pd(OAc)_2$ (6.7 mg, 0.03 mmol), $AgNO_2$ (92.3 mg, 0.6 mmol), $K_2S_2O_8$ (162.0 mg, 0.6 mmol), and anhydrous DCE (3.0 mL) was sealed in a 15 mL Schlenk flask. Then, the flask was stirred at 110 °C for 24 h. After being cooled to room temperature, the mixture was filtered with Celite and the filtrate was evaporated in vacuum; the residue was purified by flash column chromatography on silica gel with ethyl acetate/petroleum ether as the eluent to give a mixture of **2o** and **2h** in 54% yield. $^1H$ NMR analysis showed that the molar ratio of **2o**:**2h** is 75:25.

*Intermolecular Competition Experiment on **1a** and **1a-$d_5$**.* A mixture of **1a** (0.15 mmol), **1a-$d_5$** (0.15 mmol), $Pd(OAc)_2$ (6.7 mg, 0.03 mmol), $AgNO_2$ (92.3 mg, 0.6 mmol), $K_2S_2O_8$ (162.0 mg, 0.6 mmol), and anhydrous DCE (3.0 mL) was sealed in a 15 mL Schlenk flask. Then, the flask was stirred at 110 °C for 24 h. After being cooled to room temperature, the mixture was filtered with Celite and the filtrate was evaporated in vacuum; the residue was purified by flash column chromatography on silica gel with ethyl acetate/petroleum ether as the eluent to give a mixture of **2a-$d_4$** and **2a**. On the basis of the integrations related to different hydrogen resonances in $^1H$ NMR spectra, the kinetic isotope effect is calculated to be $k_H/k_D$ = 2.0.

*Nitration of 2-Phenoxypridine **1a** Catalyzed by Complex **A**.* Complex **A** was prepared according to the literature procedure.[23] The procedure for the nitration of **1a** catalyzed by **A**: **1a** (51.4 mg, 0.3 mmol), **A** (11.0 mg, 0.015 mmol), $AgNO_2$ (92.3 mg, 0.6 mmol), $K_2S_2O_8$ (162.0 mg, 0.6 mmol), phenanthrene (21.4 mg, 0.12 mmol, internal standard), and anhydrous DCE (3.0 mL) were sequentially added to a 15 mL Schlenk flask. Then, the flask was sealed and stirred at 110 °C for 48 h. Upon completion, the resulting mixture was diluted with $CH_2Cl_2$ (10 mL) and filtered through Celite. A sample was taken for GC analysis, and a 75% yield of **2a** was determined.

*Effect of Radical Scavenger TEMPO on the Nitration of **1a**.* Procedure: **1a** (51.4 mg, 0.3 mmol), $Pd(OAc)_2$ (6.7 mg, 0.03 mmol), $AgNO_2$ (92.3 mg, 0.6 mmol), $K_2S_2O_8$ (162.0 mg, 0.6 mmol), TEMPO (0.15 or 0.6 mmol), and anhydrous DCE (3.0 mL) were sequentially added to a 15 mL Schlenk flask. Then, the flask was sealed and stirred at 110 °C for 48 h. Upon completion, the resulting mixture was analyzed by GC (<10% of **2a**, TEMPO = 0.5 equiv; 0% of **2a**, TEMPO = 2 equiv).


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## ■ ASSOCIATED CONTENT

### Supporting Information

Charts for mechanistic studies as well as copies of $^{1}H$ NMR and $^{13}C$ NMR spectra of the 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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