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A 2,2′-bipyridine-palladacycle catalyzed the coupling of arylboronic acids with nitroarenes

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ABSTRACT

A novel palladium-catalyzed protocol for the synthesis of diaryl ethers derivatives has been developed. In the presence of 2,2′-bipyridine-cyclopalladated ferrocenylimine complex (Cat. Ic), diaryl ethers were selectively generated by adjusting reaction parameters through the coupling of arylboronic acids and nitroarenes with yields ranging from poor to good. The efficiency of this reaction was demonstrated by its compatibility with a range of groups. Moreover, the rigorous exclusion of air or moisture was not required in these transformations.

1. Introduction

Diaryl ethers consist of an important building block in the synthesis of natural products and pharmacological active compounds as well as polymer science target molecules.[1,2] Traditionally, the synthesis of such ethers has been accomplished via Ullmann cross-couplings, which employed aryl halides and sodium or potassium aryloxides in the presence of a stoichiometric (or greater) amount of a copper species at elevated temperatures (125–220 °C).[3] Unfortunately, these relatively harsh conditions were not well tolerated for many synthetic applications. Consequently, several modifications to the original Ullmann conditions have been developed, such as rhodium,[4] palladium,[5] copper,[6] and iron[7] catalytic systems, etc. Generally aryl halides were employed as coupling partners in these improved methods. However, several problems still remain, such as high catalyst loading, elevated temperature as well as environmentally unfriendly[8] when aryl halides were used.

Organoboron reagents are ubiquitous coupling partners due to their advantages of stability to air or moisture and good functional group tolerance.[9] To the best of our knowledge, only two examples have been described in which arylboronic acids were coupled to nitroarenes catalyzed by Rhodium[10] and copper[11] to afford diaryl ethers. However, there was no report about this transformation catalyzed by palladium when nitroarenes acted as coupling partners. Thus, the development of a method that allows a general synthesis of diaryl ethers under mild conditions, while increasing the scope of applicable substrates, would be of significant interest.

In our previous report, we have developed a 2,2′-bipyridine-palladacycle Ic catalyzed arylation of aldehydes to produce secondary alcohols in good yields in neat water using a weak acid as additive (Scheme 1, Eq. 1).[12] As continuation of our interest, herein we would like to describe the phosphine-free palladacyclic complex Ic catalyzed selective synthesis of unsymmetrical diaryl ethers by adjusting reaction parameters through the coupling of arylboronic acids and nitroarenes under basic condition (Scheme 1, Eq. 2). The results showed that palladacycle Ic exhibited high efficiency with low catalyst loading.

2. Results and discussion

Previous studies regarding the synthesis of 4-(nitrophenyl)(phenyl)-methanol **4aa** from the coupling of 4-nitrobenzaldehyde **1a** with phenylboronic acid **2a** (Scheme 2) in the presence of palladacyclic complex Ic suggested 4-phenoxybenzaldehyde **3aa** occurred as a secondary product during the catalytic transformation. Based on this discovery, we began to realize the selective generation of **3aa** in the presence of Ic by

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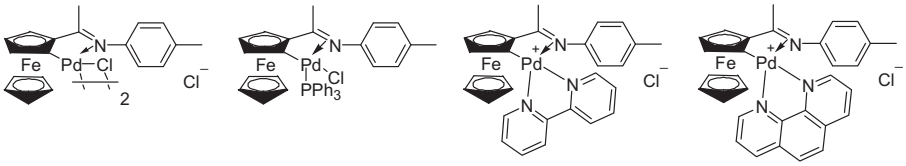
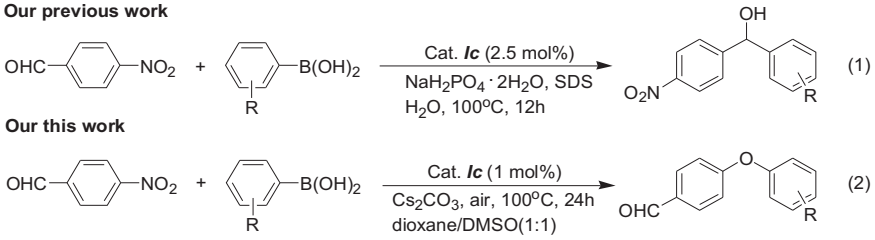
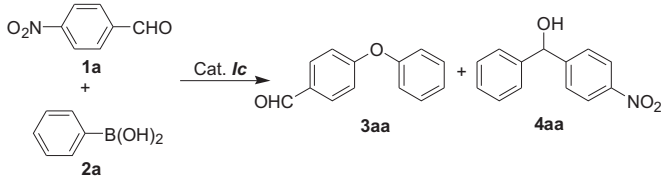




Scheme 1. Synthesis of diaryl alcohols and diaryl ethers catalyzed by Ic.

adjusting reaction parameters including palladium source, base, and solvent.

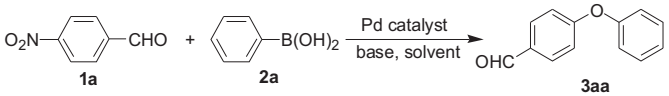


Scheme 2. Reaction of 4-nitrobenzaldehyde with phenylboronic acid.

Initial experiments were carried out by the reaction of 4-nitrobenzaldehyde **1a** with phenylboronic acid **2a** in the presence of catalyst Ic (1 mol %) when the combination of Cs_2CO_3 and DMSO was employed. To our delight, the desired product 4-phenoxybenzaldehyde **3aa** was smoothly afforded in 30% yield (Table 1, entry 1). Then we next examined the role of the solvent in this transformation. We discovered that by employing dioxane as a cosolvent in addition to DMSO (1:1), we were able to obtain biaryl ether **3aa** in consistently highest yield as compared to reactions conducted in other pure solvents, such as dioxane, toluene, DMF, CH_3NO_2, THF, and CH_3OH (Table 1, entries 1–8). As for bases tested, the use of K_2CO_3, Na_2CO_3, $CsF2H_2O$, and *t*-BuOK as bases resulted in lower yield of **3aa** (Table 1, entries 9–12 vs 8). The combination of dioxane/DMSO (1:1) and K_3PO_4 delivered **3aa** in 78% yield (Table 1, entry 13).

Among the palladium sources used including palladacyclic complex Ia–Id, $Pd(OAc)_2$, $Pd(acac)_2$, and $Pd_2(dba)_3$, 2,2′-bipyridine-palladacycle Ic exhibited the highest catalytic reactivity affording a 86% yield (Table 1, entries 8, 14–19). It is worth noting that $Pd(OAc)_2$ combined with bipyridine could be used for this transformation (Table 1, entry 20), but the yield is lower than those. So the catalyst Ic emerged as the best choice of catalyst precursors. The yields of the product decreased with decreasing the catalyst loading from 1 mol % to 0.5 mol % (Table 1, entry 21). When shortening the reaction time or reducing the reaction temperature, the yields dropped obviously (Table 1, entries 22 and 23). The yield of diaryl ether decreased with decreasing amount of phenylboronic acid (Table 1, entry 24). The excess amounts of phenylboronic acid were consumed due to the homo-coupling and protodeboronation side reactions.[13] In addition, we found that 4-phenoxybenzaldehyde (**3aa**) was isolated in a poor yield under a N_2 atmosphere (Table 1, entry 25). Furthermore, even lower yield was obtained when the

Table 1
Effect of catalysts, bases, and solvents on the selective generation of **3aa**[a]



Entry	Palladium source	Base	Solvent	Yield[b] (%)
1	Ic	Cs_2CO_3	DMSO	30
2	Ic	Cs_2CO_3	Dioxane	21
3	Ic	Cs_2CO_3	Toluene	25
4	Ic	Cs_2CO_3	DMF	55
5	Ic	Cs_2CO_3	CH_3NO_2	Trace
6	Ic	Cs_2CO_3	THF	Trace
7	Ic	Cs_2CO_3	CH_3OH	Trace
8	Ic	Cs_2CO_3	Dioxane/DMSO (1:1)	86
9	Ic	K_2CO_3	Dioxane/DMSO (1:1)	25
10	Ic	Na_2CO_3	Dioxane/DMSO (1:1)	Trace
11	Ic	$CsF·2H_2O$	Dioxane/DMSO (1:1)	10
12	Ic	*t*-BuOK	Dioxane/DMSO (1:1)	22
13	Ic	K_3PO_4	Dioxane/DMSO (1:1)	78
14	Ia	Cs_2CO_3	Dioxane/DMSO (1:1)	57
15	Ib	Cs_2CO_3	Dioxane/DMSO (1:1)	47
16	Id	Cs_2CO_3	Dioxane/DMSO (1:1)	75
17	Ia/bpy (1:4)	Cs_2CO_3	Dioxane/DMSO (1:1)	60
18	$Pd(acac)_2$	Cs_2CO_3	Dioxane/DMSO (1:1)	58
19	$Pd_2(dba)_3$	Cs_2CO_3	Dioxane/DMSO (1:1)	53
20	$Pd(OAc)_2$/bpy (1:2)	Cs_2CO_3	Dioxane/DMSO (1:1)	37
21[c]	Ic	Cs_2CO_3	Dioxane/DMSO (1:1)	58
22[d]	Ic	Cs_2CO_3	Dioxane/DMSO (1:1)	68
23[e]	Ic	Cs_2CO_3	Dioxane/DMSO (1:1)	77
24[f]	Ic	Cs_2CO_3	Dioxane/DMSO (1:1)	56
25[g]	Ic	Cs_2CO_3	Dioxane/DMSO (1:1)	12
26[h]	Ic	Cs_2CO_3	Dioxane/DMSO (1:1)	5
27[i]	Ic	Cs_2CO_3	Dioxane/DMSO (1:1)	80
28[j]	Ic	Cs_2CO_3	Dioxane/DMSO (1:1)	85

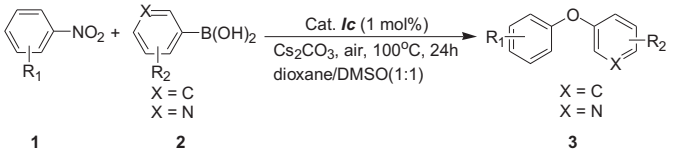
[a] Reaction conditions: **1a** (0.5 mmol), **2a** (1.5 mmol), Pd catalyst (1 mol %), base (1.0 mmol), solvent (2.0 mL), 100 °C, air, 24 h.
[b] Isolated yield.
[c] With the catalyst loading of 0.5 mol %.
[d] For 18 h.
[e] At 80 °C.
[f] Compound **2a** (1.0 mmol) was used.
[g] Under N_2.
[h] In dry dioxane/DMSO (1:1) (2.0 mL), under N_2.
[i] In dry dioxane/DMSO (1:1) (2.0 mL), under air.
[j] 5 equiv of $^{18}OH_2$ was added to dry dioxane/DMSO (1:1) (2.0 mL), **3aa**-^{18}O was formed in 6% yield.

procedure was carried out in dry dioxane and DMSO (1:1) (Table 1, entry 26). We also discovered that the yield of the product did increase to 80% yield when the model reaction was performed in the dry cosolvent (Table 1, entry 27).

To clarify the source of the oxygen in this reaction, we carried out the palladacycle-catalyzed reaction of 4-nitrobenzaldehyde **1a** with phenylboronic acid **2a** in the presence of $^{18}OH_2$ in dry dioxane and DMSO (1:1). As a result, we found that [^{18}O]-**3aa** was formed in 6% yield (Table 1, entry 28). This result suggested that most of the oxygen atom might be derived from the ambient environment.

With the optimized conditions in hand, the reactions of different nitrobenzenes with various arylboronic acids were examined to explore the scopes of the reaction. The results were shown in Table 2. To our delight, the reaction proceeded smoothly in the presence of a variety of functional groups including methoxy, chloro, bromo, formacyl, acetyl, cyano, nitro, tertiary butyl, and heterocyclic groups.

Table 2
Palladacycle Ic-catalyzed cross-coupling of nitroarenes with arylboronic acids[a]



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Entry	Ar[1] (**1**)	Ar[2] (**2**)	Product	Yield[b] (%)
1	4-CHOC$_6$H$_4$ (**1a**)	Ph (**2a**)	**3aa**	86
2	4-CHOC$_6$H$_4$ (**1a**)	2-MeC$_6$H$_4$ (**2b**)	**3ab**	69
3	4-CHOC$_6$H$_4$ (**1a**)	3-MeC$_6$H$_4$ (**2c**)	**3ac**	63
4	4-CHOC$_6$H$_4$ (**1a**)	4-MeC$_6$H$_4$ (**2d**)	**3ad**	70
5	4-CHOC$_6$H$_4$ (**1a**)	2-MeOC$_6$H$_4$ (**2e**)	**3ae**	72
6	4-CHOC$_6$H$_4$ (**1a**)	3-MeOC$_6$H$_4$ (**2f**)	**3af**	63
7	4-CHOC$_6$H$_4$ (**1a**)	4-MeOC$_6$H$_4$ (**2g**)	**3ag**	72
8	4-CHOC$_6$H$_4$ (**1a**)	4-Me$_3$CC$_6$H$_4$ (**2h**)	**3ah**	54
9	4-CHOC$_6$H$_4$ (**1a**)	2-ClC$_6$H$_4$ (**2i**)	**3ai**	62
10	4-CHOC$_6$H$_4$ (**1a**)	3-ClC$_6$H$_4$ (**2j**)	**3aj**	66
11	4-CHOC$_6$H$_4$ (**1a**)	4-ClC$_6$H$_4$ (**2k**)	**3ak**	68
12	4-CHOC$_6$H$_4$ (**1a**)	4-BrC$_6$H$_4$ (**2l**)	**3al**	52
13	4-CHOC$_6$H$_4$ (**1a**)	3-NO$_2$C$_6$H$_4$ (**2m**)	**3am**	58
14	4-CHOC$_6$H$_4$ (**1a**)	5-Phenyl-3-pyridinyl (**2n**)	**3an**	92
15	4-CHOC$_6$H$_4$ (**1a**)	5-Phenoxy-3-pyridinyl (**2o**)	**3ao**	45
16	2-CHOC$_6$H$_4$ (**1b**)	5-Phenyl-3-pyridinyl (**2n**)	**3bn**	57
17	4-MeCOC$_6$H$_4$ (**1c**)	Ph (**2a**)	**3ca**	41
18	4-CNC$_6$H$_4$ (**1d**)	Ph (**2a**)	**3da**	53
19	4-CNC$_6$H$_4$ (**1d**)	5-Phenyl-3-pyridinyl (**2n**)	**3dn**	57
20	2-CNC$_6$H$_4$ (**1e**)	Ph (**2a**)	**3ea**	76
21	2-CNC$_6$H$_4$ (**1e**)	2-MeC$_6$H$_4$ (**2b**)	**3eb**	29
22	2-CNC$_6$H$_4$ (**1e**)	4-MeC$_6$H$_4$ (**2d**)	**3ed**	83
23	2-CNC$_6$H$_4$ (**1e**)	2-MeOC$_6$H$_4$ (**2e**)	**3ee**	26
24	2-CNC$_6$H$_4$ (**1e**)	4-MeOC$_6$H$_4$ (**2g**)	**3eg**	85
25	2-CNC$_6$H$_4$ (**1e**)	4-Me$_3$CC$_6$H$_4$ (**2h**)	**3eh**	50
26	2-CNC$_6$H$_4$ (**1e**)	4-ClC$_6$H$_4$ (**2k**)	**3ek**	81
27	2-CNC$_6$H$_4$ (**1e**)	4-BrC$_6$H$_4$ (**2l**)	**3el**	72
28	2-CNC$_6$H$_4$ (**1e**)	5-Phenyl-3-pyridinyl (**2n**)	**3en**	87
29	4-CH$_3$C$_6$H$_4$ (**1f**)	Ph (**2a**)	**3fa**	92[c]
30	4-NH$_2$C$_6$H$_4$ (**1g**)	Ph (**2a**)	**3ga**	93[c]

[a] Reaction conditions: **1** (0.5 mmol), **2** (1.5 mmol), catalyst Ic (1 mol %), Cs_2CO_3 1.0 mmol, dioxane/DMSO (1:1) 2.0 mL, air, 100 °C, 24 h.
[b] Isolated yield.
[c] Biphenyl was formed.

First, the mono-substituent positions at the aryl moiety of arylboronic acids were evaluated, and the results demonstrated that the reaction was not significantly affected by the steric effect of the boronic acids (Table 2, entries 2–7). For example, the coupling of **1a** with *ortho*-, *meta*-, and *para*-methoxyboronic acid proceeded smoothly, affording the corresponding products **3ae**–**3ag** in 72%, 63%, and 72% yields, respectively. Also the electronic properties of the groups on the phenyl ring of arylboronic acids had little effect on the reaction. Generally, the arylboronic acids bearing electron-donating groups produced the corresponding products in slightly higher yields (Table 2, entries 4, 7,11, and 12). It was noteworthy that the groups such as chloro and bromo moieties in arylboronic acids **2i**–**2l**, which were commonly used for cross-coupling reactions, were all tolerated and afforded the biaryl products in moderate yields (Table 2, entries 9–12). However, using the present protocol, *m*-nitrophenylboronic acid bearing strong electron-withdrawing group reacted with **1a** to afford the respective compound **3am** in 58% yield (Table 2, entry 13). It would be specially mentioned that heterocyclic boronic acids, such as 5-phenyl-3-pyridinylboronic acid was a good partner for this coupling reaction, and the desired product **3an** was isolated in 92% yield (Table 2, entry 14).

On the other hand, different electron-deficient groups on the phenyl ring in the nitroarenes were also examined. Not only a formyl group but also other electron-deficient groups including acetyl and cyano groups delivered the desired product with yields ranging from poor to good (Table 2, entries 20–28). However, the reaction yields were sensitive to steric effects on the arylboronic acids when 2-nitro-benzonitrile was subjected to this reaction conditions. The sterically hindered *ortho*-substituted arylboronic acids were proved to be problematic for this catalyst system and gave much lower yields (Table 2, entries 21 vs 22, 23 vs 24).

In order to make a more systematic study, electron-rich groups on the phenyl ring of nitroarenes were also investigated. However, the reaction of 4-nitrotoluene (**1f**) and 4-nitroaniline (**1g**) with **2a** failed to afford the corresponding product (Table 2, entries 29 and 30). Nitroarenes with electron-deficient substituents, which would be more prone to nucleophilic attack by the pheoxide intermediate to form the diaryl ether than the analogs with electron-rich groups.

Some control experiments were carried out under the standard conditions. The results were shown in Scheme 3. The reaction of 4-hydroxybenzaldehyde (**4a**) with **2a** failed to afford the corresponding product. However, in sharp contrast, the reaction of 4-nitrobenzaldehyde (**1a**) with phenol (**5a**) gave nearly quantitative yield of the desired product **3aa** at the same conditions.

The possible mechanism for the formation of the diaryl ethers was proposed as shown in Scheme 4. First, the palladacycle was pre-activated to form **a**. Oxidative addition of nitroarene formed arylpalladium species **b**. In the presence of palladium catalyst and air, the arylboronic acid was transformed into phenoxide intermediate **c**. Then phenoxide **c** could be converted to intermediate **d** by nucleophile displacement of a nitro group. The reductive-elimination of **d** gave the diaryl ether **e** and regenerated the palladium catalyst **a**.

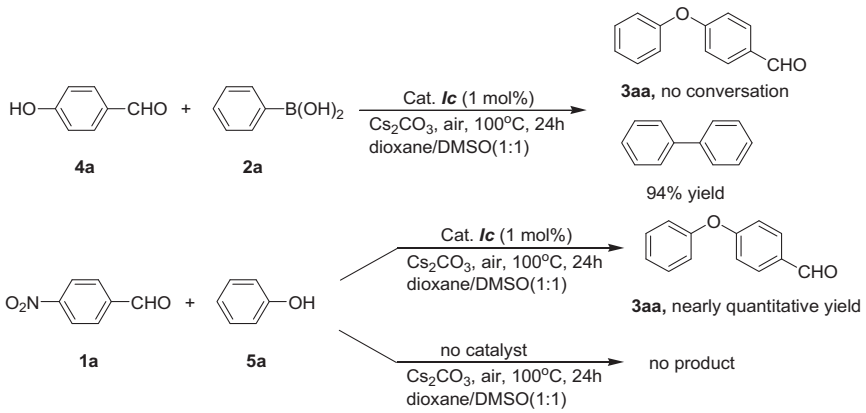
3. Conclusion

In summary, a novel palladacycle catalyzed the coupling of arylboronic acids with nitroarenes for the synthesis of unsymmetrical diaryl ethers was developed. A wide range of groups were compatible in this catalytic process. Further studies on probing the detailed mechanism and the application to organic synthesis are currently underway.

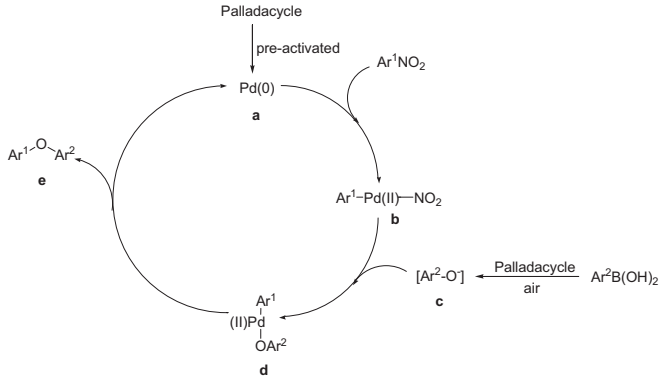
4. Experimental section

4.1. General details

^{1}H NMR, ^{13}C NMR spectra were recorded on a Bruker DPX-400 spectrometer with $CDCl_3$ as the solvent and TMS as an internal standard. Melting points were measured using a WC-1 microscopic apparatus and are uncorrected. High-resolution mass spectra were ensured on a MALDI-FTMS. GC analysis was performed on Agilent 4890D gas chromatograph. Ethyl acetate and petroleum ether (analytical grade) were used for column chromatography without further purification. Other solvents were purified according to the



Scheme 3. Control experiments.



Scheme 4. Plausible reaction mechanism.

standard methods. Other chemicals were obtained from commercial sources and used as-received unless otherwise noted.

4.2. General procedure for synthesis of 4-phenoxybenzaldehyde

A reaction vessel was charged with a mixture of phenylboronic acid (1.5 mmol), Cs_2CO_3 (1.0 mmol), catalyst Ic (1 mol %) in dioxane/DMSO (1:1) (2.0 mL), and stirred for about 20 min under air. Then 4-nitrobenzaldehyde (0.5 mmol) was then added. The mixture was heated to 100 °C and incubated in an oil bath at 100 °C for 24 h under air. After the reaction was complete, the solvent was evaporated under reduced pressure. The product **3aa** was obtained by purifying on preparative TLC, eluting with ethyl acetate/petroleum ether, and the yield was calculated based on the 4-nitrobenzaldehyde (the purified products were identified by NMR spectra and comparison of the melting points with the literature data).

*4.2.1. 4-Phenoxybenzaldehyde (**3aa**).*[7d] Light yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.02–7.07 (m, 4H), 7.20 (t, J=7.4 Hz, 1H), 7.38 (t, J=7.7 Hz, 2H), 7.81 (d, J=8.5 Hz, 2H), 9.89 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 117.5, 120.4, 124.9, 130.1, 131.2, 131.9, 155.0, 163.2, 190.7.

*4.2.2. 4-(2-Tolyloxy)benzaldehyde (**3ab**).*[14] Yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.12 (s, 3H), 6.90 (d, J=8.5 Hz, 2H), 6.95 (d, J=7.8 Hz, 1H), 7.11 (t, J=7.2 Hz, 1H), 7.17 (d, J=7.5 Hz, 1H), 7.24 (d, J=7.2 Hz, 1H), 7.77 (d, J=8.6 Hz, 2H), 9.84 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 16.4, 116.8, 121.5, 125.9, 127.9, 130.9, 131.2, 132.2, 132.4, 153.0, 163.8, 191.1.

*4.2.3. 4-(3-Tolyloxy)benzaldehyde (**3ac**).*[11] Yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.36 (s, 3H), 6.88 (d, J=9.4 Hz, 2H), 7.04 (d, J=8.1 Hz, 3H), 7.28 (t, J=7.6 Hz, 1H), 7.83 (d, J=8.4 Hz, 2H), 9.91 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.3, 117.3, 117.5, 121.0, 125.7, 129.8, 131.1, 131.9, 140.4, 155.0, 163.3, 190.8.

*4.2.4. 4-(4-Tolyloxy)benzaldehyde (**3ad**).*[11] Yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.37 (s, 3H), 6.96–7.04 (m, 4H), 7.20 (d, J=8.1 Hz, 2H), 7.82 (d, J=8.5 Hz, 2H), 9.90 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 20.8, 117.1, 120.4, 130.6, 130.9, 131.9, 134.7, 152.6, 163.6, 190.7.

*4.2.5. 4-(2-Methoxyphenoxy)benzaldehyde (**3ae**).*[11] Yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.78 (s, 3H), 6.97–7.05 (m, 4H), 7.08–7.10 (m, 1H), 7.21–7.23 (m, 1H), 7.81 (d, J=8.6 Hz, 2H), 9.89 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 55.8, 113.0, 116.2, 121.3, 122.5, 126.4, 130.8, 131.8, 142.8, 151.7, 163.5, 190.8.

*4.2.6. 4-(3-Methoxyphenoxy)benzaldehyde (**3af**).*[10] Yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.80 (s, 3H), 6.63–6.68 (m, 2H), 6.75–6.78 (m, 1H), 7.07 (d, J=8.6 Hz, 2H), 7.30 (t, J=8.1 Hz, 1H), 7.83–7.86 (m, 2H), 9.92 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 55.4, 106.3, 110.5, 112.4, 117.6, 130.5, 131.2, 131.9, 156.1, 161.1, 163.0, 190.8.

*4.2.7. 4-(4-Methoxyphenoxy)benzaldehyde (**3ag**).*[10] Yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.82 (s, 3H), 6.92–7.04 (m, 6H), 7.82 (d, J=8.6 Hz, 2H), 9.90 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 55.6, 115.1, 116.7, 121.8, 130.8, 131.9, 148.1, 156.8, 164.1, 190.8.

*4.2.8. 4-(4-(tert-Butyl)phenoxy)benzaldehyde (**3ah**).*[15] Light yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.34 (s, 9H), 7.00–7.06 (m, 4H), 7.40–7.42 (m, 2H), 7.83 (d, J=8.7 Hz, 2H), 9.91 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 31.4, 34.4, 117.2, 119.9, 126.9, 130.9, 131.9, 147.9, 152.4, 163.5, 190.8.

*4.2.9. 4-(2-Chlorophenoxy)benzaldehyde (**3ai**).*[16] Yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.00 (d, J=8.6 Hz, 2H), 7.15 (dd, J_1=1.1 Hz, J_2=8.0 Hz, 1H), 7.30–7.33 (m, 1H), 7.30–7.33 (m, 1H), 7.51 (dd, J_1=1.3 Hz, J_2=8.0 Hz, 1H), 7.85 (d, J=8.6 Hz, 2H), 9.93 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 118.0, 118.3, 120.6, 125.0, 130.9, 131.7, 132.0, 135.4, 156.0, 162.3, 190.8.

*4.2.10. 4-(3-Chlorophenoxy)benzaldehyde (**3aj**).*[17] Yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.96–6.99 (m, 1H), 7.07–7.09 (m, 3H), 7.18–7.20 (m, 1H), 7.33 (t, J=8.0 Hz, 1H), 7.87 (d, J=8.6 Hz, 2H), 9.94 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 116.6, 122.8, 126.4, 127.0, 128.4, 131.1, 131.4, 132.0, 150.4, 162.4, 190.7.

*4.2.11. 4-(4-Chlorophenoxy)benzaldehyde (**3ak**).*[11] Yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.01–7.06 (m, 4H), 7.37 (d, J=8.7 Hz, 2H), 7.85 (d, J=8.6 Hz, 2H), 9.93 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 117.6, 121.6, 130.1, 130.2, 131.5, 132.0, 153.7, 162.7, 190.7.

*4.2.12. 4-(4-Bromophenoxy)benzaldehyde (**3al**).*[11] Yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.96–6.99 (m, 2H), 7.06 (d, J=8.6 Hz, 2H),

7.50–7.54 (m, 2H), 7.86 (d, *J*=8.6 Hz, 2H), 9.93 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 117.6, 117.6, 122.0, 131.5, 132.0, 133.1, 154.2, 162.5, 190.7.

*4.2.13. 4-(3-Nitrophenoxy)benzaldehyde (**3am**).*[11] Yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.14 (d, *J*=8.5 Hz, 2H), 7.42–7.44 (m, 1H), 7.59 (t, *J*=8.1 Hz, 1H), 7.91–7.94 (m, 3H), 8.09 (d, *J*=8.2 Hz, 1H), 9.98 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 114.7, 118.6, 119.3, 125.8, 130.8, 132.2, 133.1, 149.3, 156.3, 161.3, 190.7.

*4.2.14. 4-((5-Phenyl-3-pyridinyl)oxy) benzaldehyde (**3an**).* Yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.15 (d, *J*=8.5 Hz, 2H), 7.40–7.50 (m, 3H), 7.56–7.60 (m, 3H), 7.90 (d, *J*=8.6 Hz, 2H), 8.44 (d, *J*=6.6 Hz, 1H), 8.72 (s, 1H), 9.95 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 117.9, 125.4, 127.1, 128.6, 129.1, 132.0, 132.0, 136.5, 138.1, 140.9, 144.3, 152.0, 162.1, 190.5 ppm; HRMS-ESI (positive ESI): *m*/*z* calcd for $C_{18}H_{14}NO_2$ $(M+H)^+$: 276.1019, found: 276.1029. IR (KBr pellet, cm^{-1}): 3433, 3128, 1740, 1692, 1608, 1499, 1401, 1298, 1231, 1155, 832, 765, 699.

*4.2.15. 4-((5-Phenoxy-3-pyridinyl)oxy) benzaldehyde (**3ao**).* Yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.98 (t, *J*=2.2 Hz, 1H), 7.02–7.08 (m, 4H), 7.16 (t, *J*=7.4 Hz, 1H), 7.33–7.37 (m, 2H), 7.85 (d, *J*=8.6 Hz, 2H), 8.15 (d, *J*=1.8 Hz, 1H), 8.22 (d, *J*=2.3 Hz, 1H), 9.91 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 116.6, 118.0, 119.4, 124.8, 130.2, 132.1, 132.2, 136.2, 136.8, 152.5, 155.1, 155.5, 161.7, 190.6; HRMS-ESI (positive ESI): *m*/*z* calcd for $C_{18}H_{14}NO_3$ $(M+H)^+$: 292.0968, found: 292.0977. IR (KBr pellet, cm^{-1}): 3429, 3127, 2923, 2851, 1739, 1696, 1656, 1577, 1494, 1455, 1400, 1279, 1216, 1158, 986, 831, 695.

*4.2.16. 2-((5-Phenyl-3-pyridinyl)oxy) benzaldehyde (**3bn**).* Yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.97 (d, *J*=8.3 Hz, 1H), 7.27 (t, *J*=7.6 Hz, 1H), 7.40–7.44 (m, 1H), 7.46–7.50 (m, 2H), 7.55–7.57 (m, 4H), 7.97–7.99 (dd, J_1=1.8 Hz, J_2=7.8 Hz, 1H), 8.44 (d, *J*=2.5 Hz, 1H), 8.69 (d, *J*=1.7 Hz, 1H); 10.53 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 118.4, 124.3, 124.6, 127.0, 127.2, 128.7, 129.1, 129.2, 136.0, 136.6, 138.1, 140.1, 144.0, 153.2, 158.9, 188.8; HRMS-ESI (positive ESI): *m*/*z* calcd for $C_{18}H_{14}NO_2$ $(M+H)^+$: 276.1019, found: 276.1013. IR (KBr pellet, cm^{-1}): 3424, 3130, 1740, 1674, 1626, 1565, 1514, 1448, 1400, 1298, 1222, 1186, 1156, 1098, 1023, 764, 699.

*4.2.17. 1-(4-Phenoxyphenyl)ethanone (**3ca**).*[10] Yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.57 (s, 3H), 6.95 (d, *J*=8.8 Hz, 2H), 7.07 (d, *J*=7.8 Hz, 2H), 7.20 (t, *J*=7.4 Hz, 1H), 7.39 (t, *J*=7.4 Hz, 2H), 7.94 (d, *J*=8.7 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.4, 116.2, 119.1, 123.6, 129.0, 129.5, 130.9, 154.5, 161.0, 195.7.

*4.2.18. 4-Phenoxybenzonitrile (**3da**).*[10] Light yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.99–7.08 (m, 4H), 7.21–7.25 (m, 1H), 7.41 (t, *J*=7.7 Hz, 2H), 7.60 (d, *J*=8.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 105.7, 117.8, 118.7, 120.3, 125.0, 130.1, 134.0, 154.7, 161.6.

*4.2.19. 4-((5-Phenyl-3-pyridinyl)oxy) benzonitrile (**3dn**).* Light yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.09–7.11 (m, 2H), 7.41–7.51 (m, 3H), 7.56–7.58 (m, 3H), 7.64–7.68 (m, 2H), 8.42 (d, *J*=2.5 Hz, 1H), 8.73 (d, *J*=1.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 107.0, 118.2, 118.5, 125.6, 127.2, 128.7, 129.3, 134.4, 136.5, 138.2, 140.9, 144.7, 151.8, 160.7; HRMS-ESI (positive ESI): *m*/*z* calcd for $C_{18}H_{14}NO_2$ $(M+H)^+$: 273.1022, found: 273.1020. IR (KBr pellet, cm^{-1}): 3424, 3130, 2226, 1740, 1672, 1625, 1615, 1498, 1400, 1298, 1237, 1164, 907, 835, 766, 697.

*4.2.20. 2-Phenoxybenzonitrile (**3ea**).*[18] Light yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.87 (d, *J*=8.4 Hz, 1H), 7.09–7.16 (m, 3H), 7.24 (t, *J*=7.4 Hz, 1H), 7.40–7.44 (m, 2H), 7.46–7.50 (m, 1H), 7.67 (dd, J_1=1.5 Hz, J_2=7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 103.5, 115.8, 116.7, 119.8, 122.6, 124.8, 129.9, 133.6, 134.0, 154.8, 159.6.

*4.2.21. 2-(2-Tolyloxy)benzonitrile (**3eb**).*[19] Light yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.18 (s, 3H), 6.62 (d, *J*=8.4 Hz, 1H), 6.96 (d, *J*=7.8 Hz, 1H), 7.05 (t, *J*=7.6 Hz, 1H), 7.13–7.25 (m, 3H), 7.39 (t, *J*=7.6 Hz, 1H), 7.62 (d, *J*=7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 15.9, 102.5, 115.2, 115.9, 120.6, 122.0, 125.5, 127.3, 130.3, 131.7, 133.7, 134.1, 152.4, 159.8.

*4.2.22. 2-(4-Tolyloxy)benzonitrile (**3ed**).*[20] Light yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.38 (s, 3H), 6.83 (d, *J*=8.5 Hz, 1H), 6.99 (d, *J*=8.4 Hz, 2H), 7.11 (t, *J*=7.6 Hz, 1H), 7.21 (d, *J*=8.3 Hz, 2H), 7.43–7.48 (m, 1H), 7.64–7.66 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 20.7, 103.2, 116.0, 116.3, 120.0, 122.3, 130.5, 133.7, 134.0, 134.7, 152.5, 160.2.

*4.2.23. 2-(2-Methoxyphenoxy)benzonitrile (**3ee**).*[21] Light yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.74 (s, 3H), 6.62 (d, *J*=8.5 Hz, 1H), 6.93–7.08 (m, 4H), 7.19 (t, *J*=7.6 Hz, 1H), 7.37 (t, *J*=7.8 Hz, 1H), 7.58 (d, *J*=7.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 55.8, 102.2, 113.1, 115.0, 116.1, 121.1, 121.9, 122.3, 126.5, 133.4, 133.8, 142.7, 151.5, 160.2.

*4.2.24. 2-(4-Methoxyphenoxy)benzonitrile (**3eg**).*[22] Light yellow liquid; ^{1}H NMR (400 MHz, CDCl3): δ=3.80 (s, 3H), 6.74 (d, *J*=8.4 Hz, 1H), 6.90 (d, *J*=8.8 Hz, 2H), 7.00–7.07 (m, 3H), 7.40 (t, *J*=7.6 Hz, 1H), 7.60 (d, *J*=7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 55.5, 102.7, 114.9, 115.6, 116.1, 121.5, 122.0, 133.6, 134.0, 147.8, 156.8, 160.6.

*4.2.25. 2-(4-(tert-Butyl)phenoxy)benzonitrile (**3eh**).*[23] Light yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.32 (s, 9H), 6.84 (d, *J*=8.4 Hz, 1H), 6.99 (d, *J*=8.6 Hz, 2H), 7.08 (t, *J*=7.6 Hz, 1H), 7.38–7.45 (m, 3H), 7.62 (d, *J*=7.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 31.3, 34.3, 103.3, 116.0, 116.5, 119.5, 122.3, 126.8, 133.6, 134.0, 147.9, 152.3, 160.0.

*4.2.26. 2-(4-Chlorophenoxy)benzonitrile (**3ek**).*[24] Light yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.83 (d, *J*=8.4 Hz, 1H), 6.99 (d, *J*=8.8 Hz, 2H), 7.13 (t, *J*=7.6 Hz, 1H), 7.33 (d, *J*=8.7 Hz, 2H), 7.44–7.48 (m, 1H), 7.62–7.64 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 103.8, 115.6, 116.9, 121.1, 123.1, 130.0, 130.1, 133.9, 134.2, 153.5, 159.1.

*4.2.27. 2-(4-Bromophenoxy)benzonitrile (**3el**).*[25] Light yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.87 (d, *J*=8.4 Hz, 1H), 6.96 (d, *J*=7.9 Hz, 2H), 7.16 (t, *J*=7.6 Hz, 1H), 7.49 (t, *J*=7.7 Hz, 3H), 7.66 (d, *J*=7.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 103.9, 115.6, 117.0, 117.6, 121.5, 123.2, 133.0, 113.9, 134.2, 154.1, 159.0.

*4.2.28. 2-((5-Phenyl-3-pyridinyl)oxy) benzonitrile (**3en**).* Light yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.97 (d, *J*=8.4 Hz, 1H), 7.23 (t, *J*=7.6 Hz, 1H), 7.41–7.51 (m, 3H), 7.53–7.60 (m, 4H), 7.72 (d, *J*=7.6 Hz, 1H), 8.43 (d, *J*=2.0 Hz, 1H), 8.72 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 104.3, 115.5, 117.2, 123.9, 125.3, 127.2, 128.7, 129.2, 134.2, 134.5, 136.5, 138.2, 140.4, 144.6, 152.0, 158.7; HRMS-ESI (positive ESI): *m*/*z* calcd for $C_{18}H_{14}NO_2$ $(M+H)^+$: 273.1022, found: 273.1024. IR (KBr pellet, cm^{-1}): 3428, 3129, 2229, 1740, 1659, 1565, 1514, 1482, 1446, 1401, 1296, 1241, 1183, 1158, 763, 698, 619.

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Supplementary data

Supplementary data associated with this article can be found in the online version, at http://dx.doi.org/10.1016/j.tet.2013.05.112.

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