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Rhodium or palladium-catalyzed cascade aryl addition/intramolecular lactonization of phthalaldehydonitrile to access 3-aryl and 3-alkenyl phthalides

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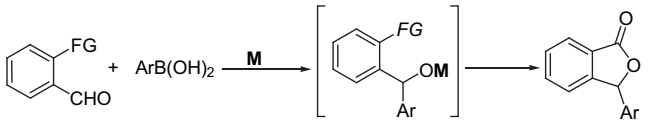
ABSTRACT

A rhodium or palladium-catalyzed addition of boronic acids to phthalaldehydonitrile, followed by an intramolecular lactonization of cyano to access 3-substituted phthalides, is described. This procedure tolerates a series of functional groups, such as methoxy, fluoro, chloro, and vinyl groups. It is a novel procedure for the synthesis of 3-arylphthalides.

1. Introduction

Phthalides frameworks are not only present in a large number of natural products and biologically active compounds,[1] but also are useful intermediates for the synthesis of tri- and tetracyclic natural products.[2] Thus, significant efforts have been focused on synthesizing phthalides in the past few decades.[3] However, the development of a simple and efficient method to access 3-arylphthalide still remains a highly desirable goal in synthetic chemistry.

Recently, some efficient approaches to obtain phthalides were developed using *ortho*-functional benzaldehyde as the substrate. In 2009, Dong reported an atom-economical approach to obtain phthalides by enantioselective hydroacylation of 2-ketoaldehydes.[4] Subsequently, Onomura demonstrated the palladium-catalyzed arylation of methyl 2-formylbenzoate with organoboronic acids for the synthesis of 3-arylphthalides.[5] Recently, Hu demonstrated the rhodium-catalyzed addition of arylboronic acids to 2-formylbenzoates afforded 3-substituted phthalides.[6] Very recently, we developed cascade aryl addition/intramolecular lactonization reactions of phthalaldehyde with organic boron catalyzed by rhodium or palladium, respectively.[7] However, some *ortho*-functional benzaldehydes were difficult to be prepared or not commercially available. Based on the aforementioned work, we envisioned the development of the transition-metal-catalyzed reaction of phthalaldehydonitrile with organoboronic acids to access 3-substituted phthalides (Scheme 1), since substituted phthalaldehydonitriles may be readily prepared from 2-bromobenzaldehyde derivatives through the transition-metal catalyzed cyanation reaction.[8] However, great challenges are remaining since the cyano group is inert to the insertion of metal species in comparison with C=O, partly due to its low polarity. Moreover, the aromatic nitriles may also have good affinity to transition-metals, resulting in the deactivation of the catalyst. For example, $PdCl_2(RCN)_2$ (R=Me, Ph)



3

FG = COOR (refs 5 and 6)
CHO (ref 7)
CN (this work)

Scheme 1. Approaches to obtain phthalides using *ortho*-functional benzaldehyde.

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are widely used as Pd catalysts. Larock[9] and Lu[10] reported carbopalladation of the nitrile to form iminopalladium intermediate, which would hydrolyze to ketones, respectively. Murakami demonstrated that organorhodium species could undergo intramolecular nucleophilic addition to nitrile to give the iminorhodium species.[11] Encouraged by their seminal works,[9–12] we report a rhodium or palladium-catalyzed reaction of phthalaldehydonitrile with organoboronic acids to give phthalides.

2. Result and discussion

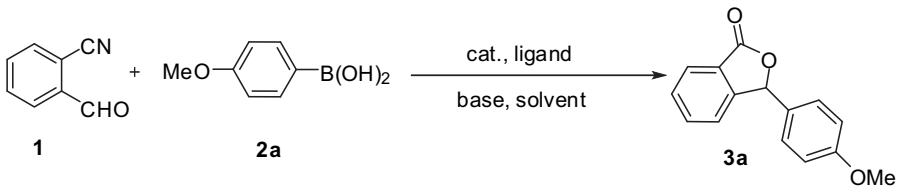
Initial studies were performed by using the reaction of phthalaldehydonitrile with 4-methoxyphenylboronic acid as the model reaction, employing $[Rh(cod)OH]_2$ as the catalyst (Table 1). The results suggested that the base played a significant role on this reaction. Li_2CO_3 was superior to other bases, such as Na_2CO_3, K_2CO_3, Cs_2CO_3, DBU, and Et_3N (Table 1, entries 1–7). The use of 1.5 equiv of Li_2CO_3 was the most effective (Table 1, entries 7–9). A series of ligands were investigated. Among the phosphines tested, such as dppp, dppe, dppb, dppf, $P(1\text{-nap})_3$, and PPh_3, dppe showed the best catalytic reactivity (Table 1, entry 9). The choice of solvent was also crucial to the catalytic reaction. The co-solvent 1,4-dioxane/H_2O appeared to be the best among the co-solvents tested (Table 1, entries 9 and 16–20). The product was not detected by GC–MS without H_2O. Next, the effect of rhodium sources was studied and $[Rh(cod)OH]_2$ possessed better catalytic activity. No product was formed in the absence of rhodium complex. Under N_2, a compatible yield was obtained (Table 1, entry 9). The reaction conducted on a 1 mmol scale produced **3a** in an acceptable 72% yield.

With the optimized conditions in hand, the scope and generality of the reaction were investigated (Table 2). The results indicated that a number of functional groups, including methoxyl, chloro, fluoro, and vinyl on the aryl moiety of boronic acids were tolerated well under the standard conditions. Generally, electron-donating boronic acids gave 3-arylphthalides in good yields. Nevertheless, the reaction became sluggish using arylboronic acids possessing electron-withdrawing groups (Table 2, entries 9 and 13). The hindrance on the phenyl ring of arylboronic acid inhibited the transformation. For example, 88% of **3a** was isolated, while the yield of **3g** dramatically decreased to 33% (Table 2, entries 1 vs 7). Particularly, (*E*)-styrylboronic acid was also a good reaction partner and 3-alkenylphthalide **3n** was isolated in moderate yield (Table 2, entry 14). Unfortunately, methylboronic acid failed to deliver the product under the standard procedure.

To probe the preliminary reaction mechanism, 2-(hydroxy(phenyl)methyl)benzonitrile was subjected to the standard procedure and **3f** was formed in 38% yield, along with 2-benzoylbenzonitrile as the byproduct. Moreover, 2-(hydroxy(phenyl)methyl)benzonitrile was detected by GC–MS when the reaction was quenched after 1 h, 2 h, and 4 h, respectively. These results indicated that 2-(hydroxy(phenyl)methyl)benzonitrile may be the intermediate in the cascade reaction.

A plausible mechanism is outlined in Scheme 2. Step (i) involves the Rh-catalyzed addition of boronic acids to C=O to form alkoxyl rhodium species **A**. In step (ii), the insertion of alkoxyl rhodium species **A** to the triple bond of the cyano group takes place to produce intermediate **B**. Then the protonolysis of intermediate **B** regenerates the catalyst Rh(I)(OH) and releases the product intermediate **C**, which encounters the hydrolysis to produce the final

Table 1
Optimization of reaction conditions[a]

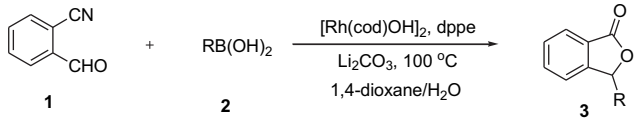


1 2a 3a

Entry	Rh source	Ligand	Base (equiv)	Solvent	Yield[b] (%)
1	$[Rh(cod)OH]_2$	dppp	Na_2CO_3 (2)	1,4-Dioxane/H_2O	59
2	$[Rh(cod)OH]_2$	dppe	Cs_2CO_3 (2)	1,4-Dioxane/H_2O	<5
3	$[Rh(cod)OH]_2$	dppe	K_3PO_4 (2)	1,4-Dioxane/H_2O	<5
4	$[Rh(cod)OH]_2$	dppe	K_2CO_3 (2)	1,4-Dioxane/H_2O	12
5	$[Rh(cod)OH]_2$	dppe	DBU (2)	1,4-Dioxane/H_2O	<5
6	$[Rh(cod)OH]_2$	dppe	Et_3N (2)	1,4-Dioxane/H_2O	30
7	$[Rh(cod)OH]_2$	dppf	Li_2CO_3 (2)	1,4-Dioxane/H_2O	66
8	$[Rh(cod)OH]_2$	dppe	Li_2CO_3 (1)	1,4-Dioxane/H_2O	80
9	$[Rh(cod)OH]_2$	dppe	Li_2CO_3 (1.5)	1,4-Dioxane/H_2O	88 (74)[c]
10	$[Rh(cod)OH]_2$	dppe	Li_2CO_3 (1.5)	1,4-Dioxane/H_2O	33
11	$[Rh(cod)OH]_2$	dppb	Li_2CO_3 (1.5)	1,4-Dioxane/H_2O	64
12	$[Rh(cod)OH]_2$	dppe	Li_2CO_3 (1.5)	1,4-Dioxane/H_2O	42
13	$[Rh(cod)OH]_2$	$(1\text{-nap})_3P$	Li_2CO_3 (1.5)	1,4-Dioxane/H_2O	34
14	$[Rh(cod)OH]_2$	PPh_3	Li_2CO_3 (1.5)	1,4-Dioxane/H_2O	34
15	$[Rh(cod)OH]_2$		Li_2CO_3 (1.5)	1,4-Dioxane/H_2O	30
18	$[Rh(cod)OH]_2$	dppe	Li_2CO_3 (1.5)	DMSO/H_2O	<5
19	$[Rh(cod)OH]_2$	dppe	Li_2CO_3 (1.5)	THF/H_2O	78
16	$[Rh(cod)OH]_2$	dppe	Li_2CO_3 (1.5)	Toluene/H_2O	<5
17	$[Rh(cod)OH]_2$	dppe	Li_2CO_3 (1.5)	DCE/H_2O	<5
20	$[Rh(cod)OH]_2$	dppe	Li_2CO_3 (1.5)	CH_3CN/H_2O	<5
21	$Rh(acac)_3$	dppe	Li_2CO_3 (1.5)	1,4-Dioxane/H_2O	<5
22	$[Rh(cod)Cl]_2$	dppe	Li_2CO_3 (1.5)	1,4-Dioxane/H_2O	40

[a] Reaction conditions: **1** (0.2 mmol), **2a** (0.3 mmol), Rh source (5 mol %), ligand (5 mol %) with indicated base in solvent/H_2O=20/1 (2 mL), 100 °C, 24 h, under air; nap=naphthyl.
[b] Isolated yield.
[c] Under N_2.

Table 2
Rhodium-catalyzed lactonization of phthalaldehydonitrile with boronic acids[a]



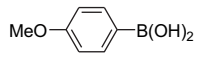
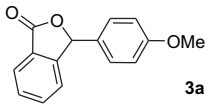
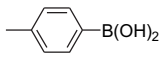
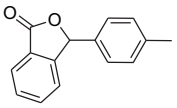
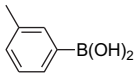
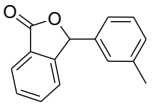
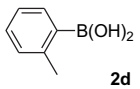
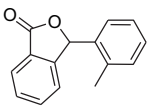
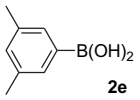
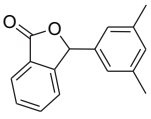
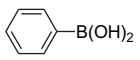
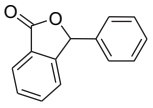
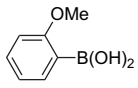
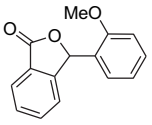
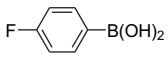
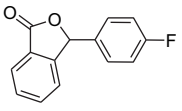
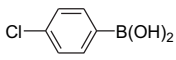
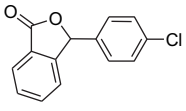
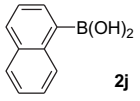
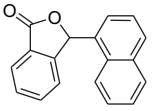
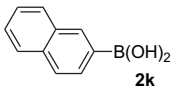
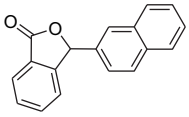
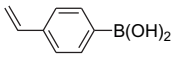
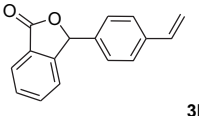
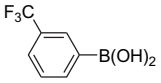
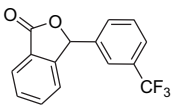
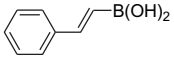
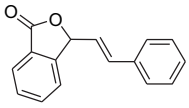
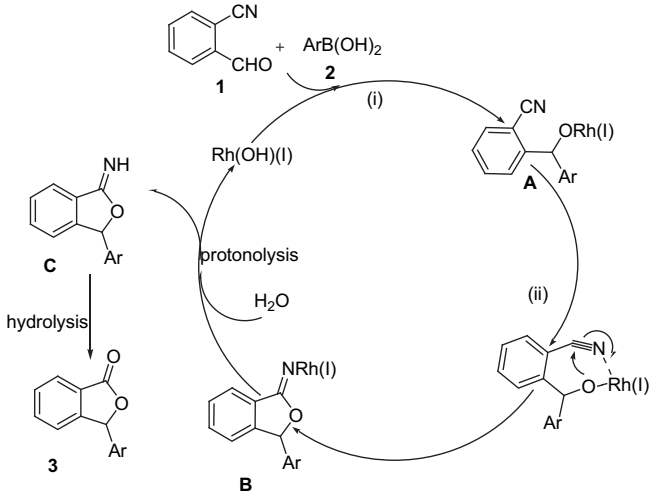
Entry	Boronic acid **2**	Product **3**	Yield[b] (%)
1	 **2a**	 **3a**	88
2	 **2b**	 **3b**	80
3	 **2c**	 **3c**	72
4	 **2d**	 **3d**	68
5	 **2e**	 **3e**	60
6	 **2f**	 **3f**	76
7	 **2g**	 **3g**	33
8	 **2h**	 **3h**	60
9	 **2i**	 **3i**	46
10	 **2j**	 **3j**	78
11	 **2k**	 **3k**	70
12	 **2l**	 **3l**	68

Table 2 (*continued*)

Entry	Boronic acid **2**	Product **3**	Yield[b] (%)
13	 **2m**	 **3m**	26
14	 **2n**	 **3n**	47

[a] Reaction conditions: **1** (0.2 mmol), **2** (0.3 mmol), $[Rh(cod)OH]_2$ (5 mol %), dppe (5 mol %), Li_2CO_3 (0.3 mmol) in 1,4-dioxane/H_2O=20/1 (2 mL), 100 °C, 24 h, under air.
[b] Isolated yield.

product **3**. Theoretical calculations at the B3LYP/6-31G*(LANL2DZ) level of theory were carried out to evaluate the possibility of the proposed mechanism in Scheme 2.[13] In calculations, the phenylboronic acid (**2**) and 2-formylbenzonitrile (**1**) were used as the model substrates, while dppe ligands were simplified to $H_2PCH_2CH_2PH_2$ (Figs. 1 and 2). It was found that the formation of LRhAr species from **2** and LRh(OH) (L=$H_2PCH_2CH_2PH_2$) is quite facile with an activation barrier of only 6.8 kcal/mol. The following generation of intermediate **A** via the addition of LRhAr to C=O moiety of **1** represents the rate-limiting step, requiring an activation free energy of 19.3 kcal/mol in the gas phase.[13] The energy needed for the intramolecular addition of alkoxyl rhodium to CN of **A** is only about 2 kcal/mol, leading to intermediate **B**, which is 22.7 kcal/mol lower in energy than the starting materials and is expected to give the final phthalide product easily under the current conditions.



Scheme 2. Plausible mechanism.

Next, we tried to develop a palladium-catalyzed lactonization of phthalaldehydonitrile with 4-methoxyphenylboronic acid. We employed $Pd(acac)_2$ as the catalyst. It was found that the choice of ligands was crucial to this catalytic reaction. The bidentate ligands were less effective for this reaction. When P(1-nap)$_3$ was employed, the best yield was obtained (Table 3, entry 6). The results are shown in Table 4. Compared to the rhodium-catalyzed lactonization with arylboronic acids, the Pd-catalyzed system is more sensitive to the electronic effect. The arylboronic acid possessing CF_3 group failed to deliver the product. The hindrance effect of the substituents on the phenyl ring of arylboronic acids was consistent with those of the Rh-catalyzed procedure.

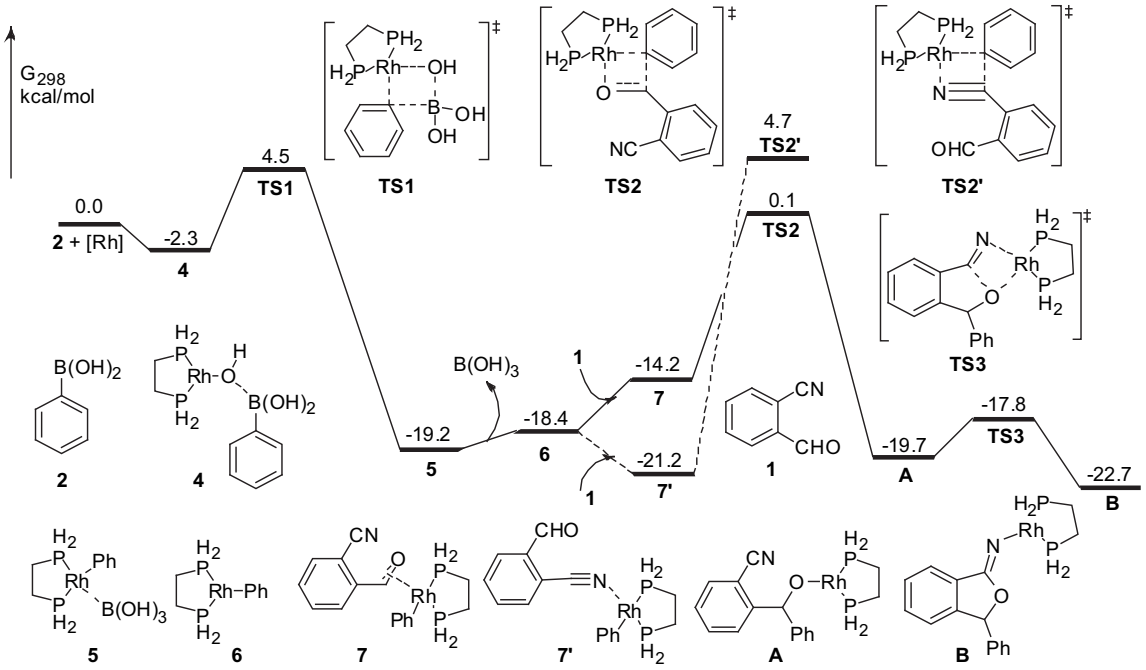


Fig. 1. Computed potential energy surface.

In summary, we have developed a novel cascade aryl addition/lactonization of phthalaldehydonitrile with boronic acids to access 3-substituted phthalides in moderate to good yields. Efforts to expand the reaction to chiral 3-aryl and alkenyl phthalides and to elucidate the mechanism in detail are underway in our laboratory.

3. Experimental section

3.1. General procedure

Chemicals were either purchased or purified by standard techniques without special instructions. ^{1}H NMR and ^{13}C NMR spectra were measured on a 500 MHz Bruker spectrometer (^{1}H 500 MHz, ^{13}C 125 MHz), using $CDCl_3$ as the solvent with tetramethylsilane (TMS) as the internal standard at room temperature. Chemical shifts (δ) are given in parts per million relative to TMS, the coupling constants J are given in hertz. Column chromatography was performed using EM Silica gel 60 (300–400 mesh).

3.2. Typical experimental procedure for rhodium-catalyzed lactonization of phthalaldehydonitrile with boronic acids

Under air, a reaction tube was charged with phthalaldehydonitrile (26.2 mg, 0.2 mmol), boronic acid (0.3 mmol), $[Rh(cod)OH]_2$ (4.6 mg, 5 mol %), dppe (4.0 mg, 5 mol %), and 1.4-dioxane/H_2O=20/1 (2 mL). The mixture was stirred at 100 °C. After the mixture was stirred for 24 h, the solvent was evaporated under reduced pressure and the residue was purified by flash column chromatography on silica gel to give the product.

3.3. Typical experimental procedure for palladium-catalyzed lactonization of phthalaldehydonitrile with boronic acids

Under air, a reaction tube was charged with phthalaldehydonitrile (26.2 mg, 0.2 mmol), boronic acid (0.6 mmol), $Pd(acac)_2$ (3.0 mg, 5 mol %), P(1-nap)$_3$ (4.2 mg, 5 mol %), and toluene/H_2O=40/1 (2 mL). The mixture was stirred at 100 °C. After the

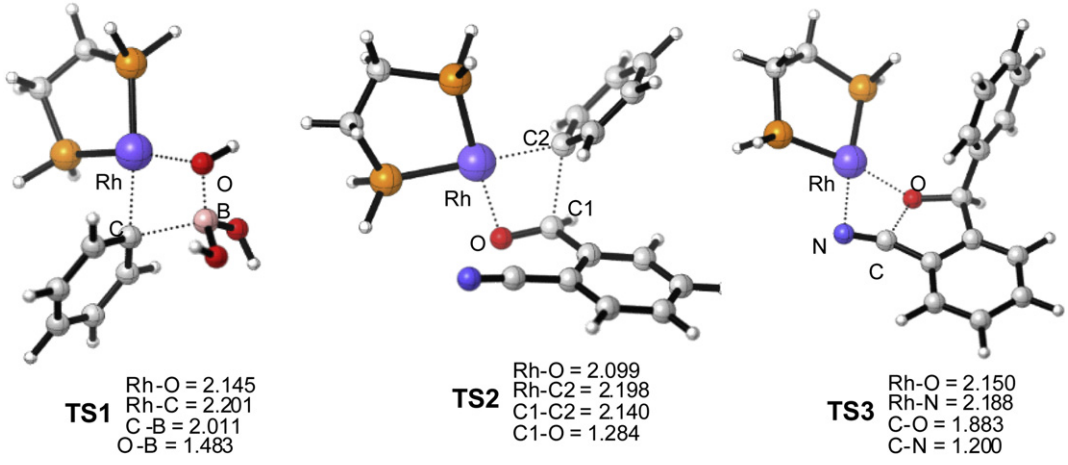
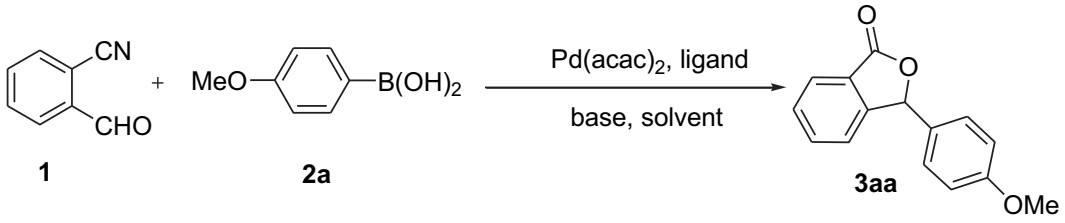


Fig. 2. Geometric structures for **TS1**, **TS2**, and **TS3**, selected distances are in angstrom.

Table 3
Screening conditions for palladium-catalyzed lactonization of phthalaldehydonitrile with 4-methoxyphenylboronic acid[a]



Entry	Ligand	Base	Solvent	Yield[b] (%)
1	dppe	$NaHCO_3$	Toluene/H_2O	<5
2	dppb	$NaHCO_3$	Toluene/H_2O	<5
3	dppf	$NaHCO_3$	Toluene/H_2O	<5
4	dppp	$NaHCO_3$	Toluene/H_2O	<5
5	PPh[a]	$NaHCO_3$	Toluene/H_2O	<5
6	$(1\text{-nap})_3P$	$NaHCO_3$	Toluene/H_2O	87
7	$(1\text{-nap})_3P$	$NaHCO_3$	THF/H_2O	28
8	$(1\text{-nap})_3P$	$NaHCO_3$	1,4-Dioxane/H_2O	59
9	$(1\text{-nap})_3P$	$NaHCO_3$	DMF/H_2O	<5
10	$(1\text{-nap})_3P$	$NaHCO_3$	DMSO/H_2O	<5
11	$(1\text{-nap})_3P$	$NaHCO_3$	CH_3CN/H_2O	44
12	$(1\text{-nap})_3P$	$NaHCO_3$	DCE/H_2O	68
15	$(1\text{-nap})_3P$	Li_2CO_3	Toluene/H_2O	66
16	$(1\text{-nap})_3P$	Na_2CO_3	Toluene/H_2O	39
13	$(1\text{-nap})_3P$	K_2CO_3	Toluene/H_2O	21
14	$(1\text{-nap})_3P$	Cs_2CO_3	Toluene/H_2O	<5
17	$(1\text{-nap})_3P$	$KHCO_3$	Toluene/H_2O	48
18	$(1\text{-nap})_3P$	Et_3N	Toluene/H_2O	32

[a] Reaction conditions: **1** (0.2 mmol), **2a** (0.6 mmol), $Pd(acac)_2$ (5 mol %), ligand (5 mol %) with indicated base in solvent/H_2O=40/1 (2 mL), 100 °C, 24 h, under air; nap=naphthyl.
[b] Isolated yield.

mixture was stirred for 24 h, the solvent was evaporated under reduced pressure and the residue was purified by flash column chromatography on silica gel to give the product.

*3.3.1. 3-(4-Methoxyphenyl)isobenzofuran-1(3H)-one (**3a**)*[14]. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.89 (d, J=7.6 Hz, 1H), 7.59–7.56 (m, 1H), 7.50–7.47 (m, 1H), 7.24 (d, J=7.7 Hz, 1H), 7.10 (d, J=8.6 Hz, 2H), 6.82 (d, J=8.6 Hz, 2H), 6.30 (s, 1H), 3.73 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 170.5, 160.4, 149.8, 134.2, 129.3, 128.8, 128.3, 125.9, 125.6, 122.9, 114.3, 82.7, 55.3.

*3.3.2. 3-p-Tolylisobenzofuran-1(3H)-one (**3b**)*[7]. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.89 (d, J=7.7 Hz, 1H), 7.59–7.56 (m, 1H), 7.49–7.46 (m, 1H), 7.25 (d, J=7.7 Hz, 1H), 7.11 (d, J=8.1 Hz, 2H), 7.08 (d, J=8.1 Hz, 2H), 6.31 (s, 1H), 2.28 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 170.6, 149.8, 139.3, 134.2, 133.4, 129.6, 129.3, 127.0, 125.7, 125.6, 122.8, 82.8, 21.2.

*3.3.3. 3-m-Tolylisobenzofuran-1(3H)-one (**3c**)*[15]. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.89 (d, J=7.5 Hz, 1H), 7.59–7.56 (m, 1H), 7.49–7.46 (m, 1H), 7.27–7.25 (m, 1H), 7.21–7.18 (m, 1H), 7.10 (d, J=7.5 Hz, 1H), 7.01–6.99 (m, 2H), 6.30 (s, 1H), 2.23 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 170.6, 149.8, 138.8, 136.3, 134.3, 130.0, 129.3, 128.8, 127.5, 125.6, 124.0, 122.8, 82.8, 21.3.

*3.3.4. 3-o-Tolylisobenzofuran-1(3H)-one (**3d**)*[16]. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.91 (d, J=7.7 Hz, 1H), 7.62–7.60 (m, 1H), 7.60–7.59 (m, 1H), 7.52–7.49 (m, 1H), 7.28–7.18 (m, 3H), 6.85 (d. J=7.8 Hz, 1H), 6.62 (s, 1H), 2.43 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 170.6, 149.3, 137.2, 134.2, 134.1, 131.1, 129.4, 129.3, 127.3, 126.5, 126.4, 125.8, 123.0, 80.5, 19.3.

*3.3.5. 3-(3,5-Dimethylphenyl)isobenzofuran-1(3H)-one (**3e**)*[7]. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.89 (d, J=7.7 Hz, 1H), 7.57–7.56 (m, 1H), 7.49–7.48 (m, 1H), 7.27 (d, J=7.7 Hz, 1H), 6.93 (s, 1H), 6.80 (s, 2H), 6.26 (s, 1H), 2.22 (s, 6H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 170.6, 149.9, 138.6, 136.2, 134.2, 130.9, 129.2, 125.5, 125.5, 124.6, 122.8, 82.8, 21.2.

*3.3.6. 3-Phenylisobenzofuran-1(3H)-one (**3f**)*[17]. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.90 (d, J=7.5 Hz, 1H), 7.59–7.56 (m, 1H), 7.50–7.47 (m, 1H), 7.32–7.19 (m, 6H), 6.34 (s, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 170.5, 149.7, 136.4, 134.3, 129.3, 129.3, 128.9, 126.9, 125.6, 125.6, 122.8, 82.7.

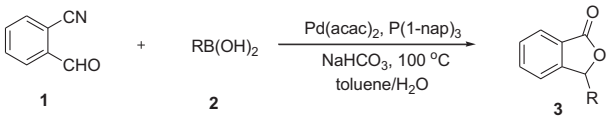
*3.3.7. 3-(2-Methoxyphenyl)isobenzofuran-1(3H)-one (**3g**)*[3l]. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.86 (d, J=7.6 Hz, 1H), 7.55–7.52 (m, 1H), 7.44 (t, J=7.5 Hz, 1H), 7.37 (d, J=7.7 Hz, 1H), 7.27–7.24 (m, 1H), 7.02–7.00 (m, 1H), 6.90 (d, J=8.3 Hz, 1H), 6.84 (t, J=7.5 Hz, 1H), 6.79 (s, 1H), 3.84 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 171.0, 157.0, 150.4, 134.1, 130.1, 129.0, 126.9, 125.7, 125.4, 125.0, 122.9, 120.9, 111.0, 78.1, 55.6.

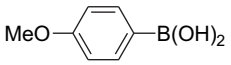
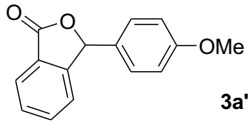
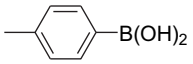
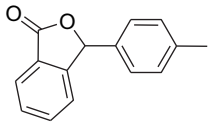
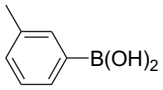
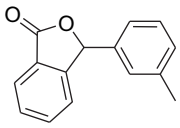
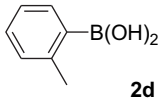
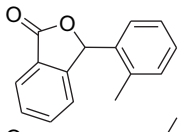
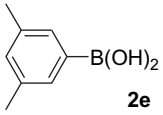
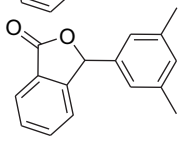
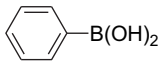
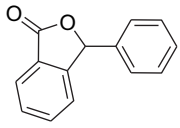
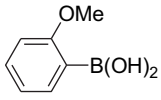
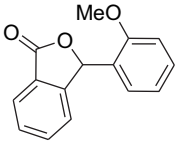
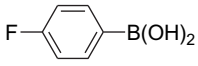
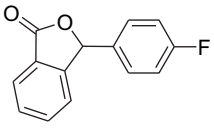
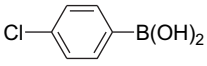
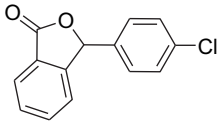
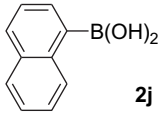
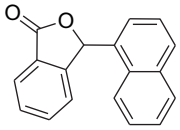
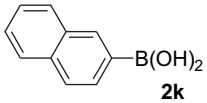
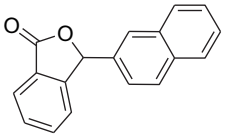
*3.3.8. 3-(4-Fluorophenyl)isobenzofuran-1(3H)-one (**3h**)*[7]. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.90 (d, J=7.5 Hz, 1H), 7.61–7.58 (m, 1H), 7.52–7.49 (m, 1H), 7.25 (d, J=7.5 Hz, 1H), 7.20–7.16 (m, 2H), 7.02–6.98 (m, 2H), 6.32 (s, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 170.2, 163.2 (d, J=247.3 Hz), 149.4, 134.4, 132.2, 129.5, 129.0 (d, J=8.4 Hz), 125.7, 125.6, 122.8, 116.0 (d, J=21.8 Hz), 82.0.

*3.3.9. 3-(4-Chlorophenyl)isobenzofuran-1(3H)-one (**3i**)*[3m]. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.97 (d, J=7.7 Hz, 1H) 7.68–7.64 (m, 1H), 7.59–7.56 (m, 1H), 7.37–7.21 (m, 5H), 6.37 (s, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 170.2, 149.2, 135.3, 135.0, 134.4, 129.6, 129.2, 128.4, 125.8, 125.6, 122.7, 81.8.

*3.3.10. 3-(Naphthalen-1-yl)isobenzofuran-1(3H)-one (**3j**)*[3l]. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.16 (d, J=8.5 Hz, 1H), 7.94 (d, J=7.6 Hz, 1H), 7.85 (d, J=8.1 Hz, 1H), 7.80 (d, J=8.1 Hz, 1H), 7.58–7.48 (m, 4H), 7.36–7.30 (m, 2H), 7.18–7.17 (m, 2H). ^{13}C NMR ($CDCl_3$, 125 MHz):

Table 4
Palladium-catalyzed lactonization of phthalaldehydonitrile with boronic acids



Entry	Boronic acid **2**	Product **3**	Yield[a] (%)
1	 **2a**	 **3a'**	88
2	 **2b**	 **3b'**	80
3	 **2c**	 **3c'**	72
4	 **2d**	 **3d'**	90
5	 **2e**	 **3e'**	82
6	 **2f**	 **3f'**	70
7	 **2g**	 **3g'**	34
8	 **2h**	 **3h'**	60
9	 **2i**	 **3i'**	54
10	 **2j**	 **3j'**	71
11	 **2k**	 **3k'**	60

[a] Reaction conditions: **1** (0.2 mmol), **2** (0.6 mmol), $Pd(acac)_2$ (5 mol %), $P(1\text{-nap})_3$ (5 mol %), $NaHCO_3$ (0.6 mmol) in toluene/H_2O=40/1 (2 mL), 100 °C, 24 h, under air. Isolated yield.

δ 170.5, 149.3, 134.1, 134.0, 131.9, 131.3, 129.9, 129.5, 129.0, 127.0, 126.2, 126.1, 126.0, 125.2, 124.5, 123.2, 122.9, 79.6.

*3.3.11. 3-(Naphthalen-2-yl)isobenzofuran-1(3H)-one (**3k**)*[7]. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.94 (d, J=7.7 Hz, 1H), 7.79–7.76 (m, 4H), 7.59–7.44 (m, 4H), 7.28 (dd, J_1=7.7 Hz, J_2=0.8 Hz, 1H), 7.17 (dd, J_1=8.5 Hz, J_2=1.7 Hz, 1H), 6.50 (s, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 170.0, 149.7, 134.4, 133.7, 133.6, 133.1, 129.4, 129.1, 128.1, 127.8, 126.8, 126.7, 126.6, 125.7, 125.6, 123.8, 122.9, 82.9.

*3.3.12. 3-(4-Vinylphenyl)isobenzofuran-1(3H)-one (**3l**)*[7]. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.90 (d, J=7.7 Hz, 1H), 7.60–7.57 (m, 1H), 7.50–7.47 (m, 1H), 7.34 (m, 2H), 7.26 (dd, J_1=7.7 Hz, J_2=0.8 Hz, 1H), 7.16 (d, J=8.3 Hz, 2H), 6.63 (dd, J_1=17.5 Hz, J_2=10.9 Hz, 1H), 6.33 (s, 1H), 5.70 (dd, J_1=17.5 Hz, J_2=0.6 Hz, 1H), 5.22 (dd, J_1=10.9 Hz, J_2=0.6 Hz, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 170.5, 149.6, 138.7, 136.0, 135.7, 134.3, 129.4, 127.6, 127.2, 126.7, 125.7, 125.6, 122.8, 115.0, 82.5.

*3.3.13. 3-(3-(Trifluoromethyl)phenyl)isobenzofuran-1(3H)-one (**3m**)*[18]. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.93 (d, J=7.5 Hz, 1H), 7.64–7.57 (m, 2H), 7.54–7.40 (m, 4H), 7.28 (d, J=7.8 Hz, 1H), 6.39 (s, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 170.0, 148.9, 137.6, 134.6, 131.3 (q, J_{C-F}=27.2 Hz), 130.1, 126.1 (q, J_{C-F}=3.8 Hz), 125.4, 124.8, 123.8 (q, J_{C-F}=270.2 Hz), 123.7 (q, J_{C-F}=3.8 Hz), 81.6.

*3.3.14. (E)-3-Styrylisobenzofuran-1(3H)-one (**3n**)*[3l]. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.87 (d, J=7.7 Hz, 1H), 7.64–7.61 (m, 1H), 7.50–7.48 (m, 1H), 7.40–7.22 (m, 6H), 6.84 (d, J=15.7 Hz, 1H), 6.07 (dd, J_1=15.7 Hz, J_2=7.9 Hz, 1H), 5.94 (d, J=7.9 Hz, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 170.3, 148.8, 135.4, 135.2, 134.2, 129.4, 128.7, 128.6, 126.9, 125.9, 125.8, 123.9, 122.7, 82.0.

*3.3.15. 3-(4-Methoxyphenyl)isobenzofuran-1(3H)-one (**3a′**)*[14]. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.88 (d, J=7.5 Hz, 1H), 7.59–7.56 (m, 1H), 7.50–7.46 (m, 1H), 7.24 (d, J=8.0 Hz, 1H), 7.10 (dd, J_1=11.5 Hz, J_2=3.0 Hz, 2H), 6.81 (d, J=8.5 Hz, 2H), 6.30 (s, 1H), 3.73 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 170.5, 160.4, 149.8, 134.2, 129.3, 128.8, 128.3, 125.9, 125.6, 122.9, 114.3, 82.7, 55.3.

*3.3.16. 3-p-Tolylisobenzofuran-1(3H)-one (**3b′**)*[7]. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.88 (d, J=7.5 Hz, 1H), 7.58–7.54 (m, 1H), 7.49–7.45 (m, 1H), 7.24 (d, J=7.5 Hz, 1H), 7.10 (d, J=8.0 Hz, 2H), 7.07 (d, J=8.0 Hz, 2H), 6.29 (s, 1H), 2.27 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 170.6, 149.8, 139.3, 134.2, 133.4, 129.6, 129.2, 127.0, 125.7, 125.5, 122.8, 82.8, 21.2.

*3.3.17. 3-m-Tolylisobenzofuran-1(3H)-one (**3c′**)*[15]. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.89 (d, J=7.5 Hz, 1H), 7.59–7.56 (m, 1H), 7.49–7.46 (m, 1H), 7.27–7.25 (m, 1H), 7.21–7.18 (m, 1H), 7.10 (d, J=7.5 Hz, 1H), 7.01–6.99 (m, 2H), 6.30 (s, 1H), 2.23 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 170.6, 149.8, 138.8, 136.3, 134.3, 130.0, 129.3, 128.8, 127.5, 125.6, 124.0, 122.8, 82.8, 21.3.

*3.3.18. 3-o-Tolylisobenzofuran-1(3H)-one (**3d′**)*[16]. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.89 (d, J=8.0 Hz, 1H), 7.60–7.57 (m, 1H), 7.50–7.47 (m, 1H), 7.26 (d, J=8.0, 1H), 7.19–7.16 (m, 2H), 7.06–7.02(m, 1H), 6.83 (d, J=8.0 Hz, 1H), 6.59 (s, 1H), 2.41 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 170.5, 149.2, 137.1, 134.1, 134.0, 131.1, 129.3, 129.3, 127.2, 126.4, 125.7, 123.0, 80.5, 19.3.

*3.3.19. 3-(3,5-Dimethylphenyl)isobenzofuran-1(3H)-one (**3e′**)*[7]. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.89 (d, J=7.5 Hz, 1H), 7.59–7.56 (m, 1H), 7.50–7.48 (m, 1H), 7.27 (d, J=8.0 Hz, 1H), 6.93 (s, 1H), 6.80 (s, 2H), 6.26 (s, 1H), 2.22 (s, 6H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 170.6, 149.9, 138.6, 136.2, 134.2, 130.9, 129.2, 125.5, 125.5, 124.6, 122.8, 82.8, 21.2.

*3.3.20. 3-Phenylisobenzofuran-1(3H)-one (**3f′**)*[17]. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.96 (d, J=7.5 Hz, 1H), 7.66–7.63 (m, 1H), 7.57–7.54 (m, 1H), 7.38–7.27 (m, 6H), 6.41 (s, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 170.5, 149.7, 136.4, 134.3, 129.3, 129.3, 129.0, 127.0, 125.6, 125.6, 122.8, 82.7.

*3.3.21. 3-(2-Methoxyphenyl)isobenzofuran-1(3H)-one (**3g′**)*[3l]. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.86 (d, J=7.7 Hz, 1H), 7.55–7.52 (m, 1H), 7.44 (t, J=7.5 Hz, 1H), 7.37 (d, J=7.6 Hz, 1H), 7.27–7.23 (m, 1H), 7.02–7.00 (m, 1H), 6.89 (d, J=8.3 Hz, 1H), 6.83 (t, J=7.5 Hz, 1H), 6.78 (s, 1H), 3.84 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 171.0, 157.0, 150.4, 134.1, 130.1, 129.0, 126.9, 125.7, 125.4, 125.0, 122.9, 120.9, 111.0, 78.1, 55.6.

*3.3.22. 3-(4-Fluorophenyl)isobenzofuran-1(3H)-one (**3h′**)*[7]. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.90 (d, J=7.5 Hz, 1H), 7.61–7.58 (m, 1H), 7.52–7.49 (m, 1H), 7.25 (d, J=7.5 Hz, 1H), 7.20–7.17 (m, 2H), 7.02–6.98 (m, 2H), 6.32 (s, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 170.3, 163.2 (d, J=234.3 Hz), 149.4, 134.4, 132.3, 129.5, 129.1 (d, J=8.5 Hz), 125.8, 125.7, 122.8, 116.0 (d, J=21.8 Hz), 82.0.

*3.3.23. 3-(4-Chlorophenyl)isobenzofuran-1(3H)-one (**3i′**)*[3m]. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.90 (d, J=8.0 Hz, 1H), 7.61–7.58 (m, 1H), 7.52–7.49 (m, 1H), 7.30–7.14 (m, 5H), 6.31 (s, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 170.2, 149.2, 135.3, 135.0, 134.4, 129.6, 129.2, 128.4, 125.8, 125.6, 122.7, 81.8.

*3.3.24. 3-(Naphthalen-1-yl)isobenzofuran-1(3H)-one (**3j′**)*[3l]. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.16 (d, J=8.5 Hz, 1H), 7.93 (d, J=7.7 Hz, 1H), 7.85 (d, J=8.1 Hz, 1H), 7.79 (d, J=8.1 Hz, 1H), 7.57–7.48 (m, 4H), 7.36–7.29 (m, 2H), 7.18–7.16 (m, 2H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 170.5, 149.3, 134.1, 134.0, 131.9, 131.3, 129.9, 129.5, 129.0, 127.0, 126.2, 126.1, 126.0, 125.2, 124.5, 123.2, 122.9, 79.7.

*3.3.25. 3-(Naphthalen-2-yl)isobenzofuran-1(3H)-one (**3k′**)*[7]. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.01 (d, J=7.5 Hz, 1H), 7.86–7.83 (m, 4H), 7.68–7.51 (m, 4H), 7.34 (d, J=8.0, 1H), 7.24 (d, J=8.5 Hz, 1H), 6.60 (s, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 170.0, 149.7, 134.4, 133.7, 133.6, 133.1, 129.4, 129.1, 128.1, 127.8, 126.8, 126.7, 126.7, 125.7, 125.7, 123.8, 122.9, 82.9.

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Supplementary data

Supplementary data associated with this article can be found in online version at doi:10.1016/j.tet.2011.04.100.

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