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Tandem addition/cyclization for synthesis of 2-aroyl benzofurans and 2-aroyl indoles by carbopalladation of nitriles†

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The first example of the palladium-catalyzed tandem addition/cyclization of 2-(2-acylphenoxy)acetonitriles with arylboronic acids has been developed, providing a new strategy for the synthesis of 2-aroyl benzofurans with excellent chemoselectivity and wide functional group compatibility. Preliminary mechanistic experiments indicate that this tandem process involves sequential nucleophilic addition generating 2-(2-acylphenoxy)-1-phenylethan-1-one followed by an intramolecular cyclization. This methodology has also been applied to the synthesis of 2-aroyl indoles and the potent CYP19 inhibitor 1-(benzofuran-2-yl(phenyl)methyl)-1*H*-1,2,4-triazole.

Introduction

Owing to the inherently inert nature of the C≡N bond, nitriles, such as acetonitrile and benzonitrile, have been usually used as solvents or ligands in organometallic reactions.[1] The development of inert cyano group activation/carbon–carbon or carbon–heteroatom bond forming reactions catalyzed by transition metals has attracted a great deal of attention recently.[2] A wide range of efficient transition metal-catalyzed transformations of nitriles have been achieved with organoboron reagents[3] since the pioneering work on the addition of arylpalladium species to the cyano group reported by Larock and co-workers.[4] In recent years, our group has also achieved a number of palladium-catalyzed tandem reactions of nitriles with organoboron reagents for access to alkyl aryl ketones, diketones, 2-aminobenzophenones, indoles, isoquinolines, isoquinolones, quinazolines.[5] The scope of this chemistry has been expanded to other coupling partners, including sodium aryl sulfinates or arylsulfinic acids,[6] aryl halides,[7] benzoic acids,[8] arylhydrazines,[9] and arylsulfonyl hydrazides.[10]

Benzofurans are important structural motifs because of their ubiquity in natural products, pharmaceuticals, and materials.[11] In particular, 2-aroyl benzofurans and their derivatives have become increasingly noticed in the past few years because they are an important class of heterocycles found in bioactive natural products and biologically active molecules, such as Rugchalcone A, Rugchalcone B and 1-(benzofuran-2-yl(phenyl)methyl)-1*H*-1,2,4-triazole (Fig. 1).[12] Hence, effective methods for the construction of benzofurans have been actively pursued during the past several decades.[13] Although transformation of nitriles into various functional groups has been well-established, only sporadic examples of the tandem reaction of the readily available nitriles for access to benzofurans have been reported to date. For examples, Lu's group[14] (Scheme 1a) and our group[5a] (Scheme 1b) have developed synthesis of benzofurans by Pd-catalyzed addition of arylboronic acids or sodium sulfinates to functionalized nitriles.

In addition, because the highly reactive formyl group was easier to take place nucleophilic addition than that of the inert cyano group (Scheme 1c), controlling the chemoselectivity to avoid the addition reaction of arylboronic acid to formyl group is often difficult when multiple functional groups such as formyl group and cyano group are simultaneously present in the substrates.[15] For examples, in this Pd-catalyzed addition of phenylboronic acid to 4-formylbenzonitrile, the cyano group remains intact while the 4-(hydroxy(phenyl)methyl)benzonitrile is obtained *via* addition to the formyl group in high

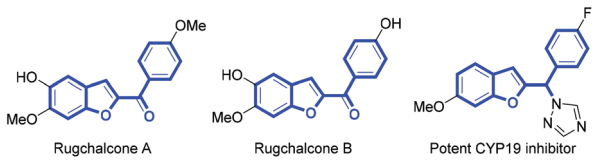

Fig. 1 Representative bioactive 2-aroyl benzofuran and its derivative.

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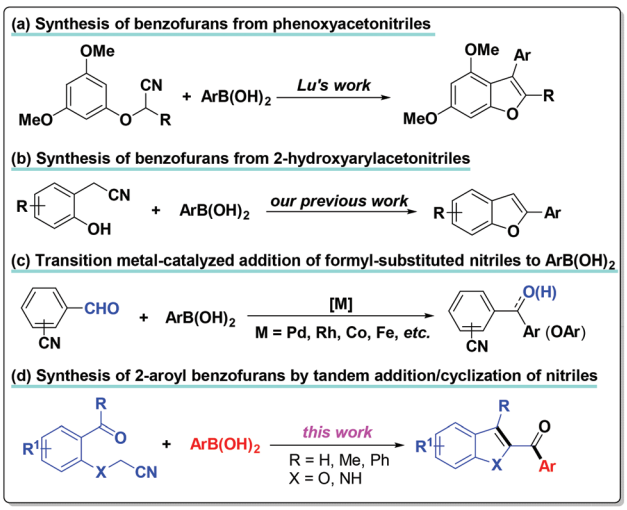


Scheme 1 Design of new approach to 2-aroyl benzofurans.

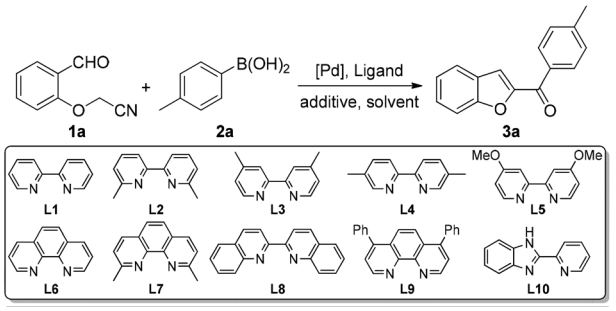
yield.[15a,e,f] Therefore, the development of a practical and general approach to benzofurans using formyl-substituted nitriles as substrates remains a challenging area for exploration. This work is part of the continuing efforts in our laboratory toward the development of novel transition metal-catalyzed transformations of nitriles.[5] Herein, we report the first example of palladium-catalyzed tandem addition/cyclization of 2-(2-acylphenoxy)acetonitriles with arylboronic acids for the synthesis of structurally diverse 2-aroyl benzofurans with excellent chemoselectivity and wide functional group compatibility (Scheme 1d). This methodology has also been applied to the synthesis of 2-aroyl indoles and the potent CYP19 inhibitor 1-(benzofuran-2-yl(phenyl)methyl)-1*H*-1,2,4-triazole.

Results and discussion

Our study commenced by examining the reaction of readily available 2-(2-formylphenoxy)acetonitrile (**1a**) with *p*-tolylboronic acid (**2a**) for the screening of reaction conditions (Table 1). Trace amount of the desired product benzofuran-2-yl(*p*-tolyl) methanone (**3a**) was detected by GC/MS analysis when the combination of $PdCl_2$, trifluoroacetic acid (TFA) and 2,2′-bipyridine (**L1**) was used in THF (entry 1). We were pleased to find that the yield of **3a** could be improved to 62% using $Pd(TFA)_2$ as a catalyst (entries 2–6). Among bidentate nitrogen ligands (**L1–L10**), sterically bulky ligands 6,6′-dimethyl-2,2′-bipyridine (**L2**), 2,9-dimethyl-1,10-phenanthroline (**L7**) and 2,2′-biquinoline (**L8**) were found to efficiently promoted the reaction and afforded the desired product **3a** in 84%, 71% and 74% yields, respectively (entries 7, 12 and 13). **L2** was the most effective and gave **3a** in 84% yield (entry 7). Other ligands, including 4,4′-dimethyl-2,2′-bipyridine (**L3**), 5,5′-dimethyl-2,2′-bipyridine (**L4**), 4,4′-dimethoxy-2,2′-bipyridine (**L5**), 1,10-phenanthroline (**L6**), 4,7-diphenyl-1,10-phenanthroline (**L9**) and 2-(pyridin-2-yl)-1*H*-benzo[*d*]imidazole (**L10**), were less efficient (entries 8–11, 14 and 15). Replacement of TFA with other acids, including *p*-toluenesulfonic acid monohydrate ($TsOH{\cdot}H_2O$), CH_3CO_2H $PhCO_2H$, CF_3SO_3H, resulted in relatively lower yields (entries 16–19). This reaction did not work using HCl or $ZnCl_2$ as an additive (entries 20 and 21). An investigation of the effect of solvents (entries 7, 22–27) revealed that use of 2-methyltetrahydrofuran (2-MeTHF) as a green solvent increased the yield of **3a** to 92% (entry 27). The role of the 2-MeTHF in the reaction is not clear. 2-MeTHF is known to be a unique solvent as a valuable alternative to the normally used ethereal solvents in organic synthesis.[16] The desired product **3a** was not detected if either palladium catalyst or ligand was absent (entries 28 and 29).

With the optimized conditions in hand, we next sought to investigate the substrate scope (Table 2). First, a wide range of

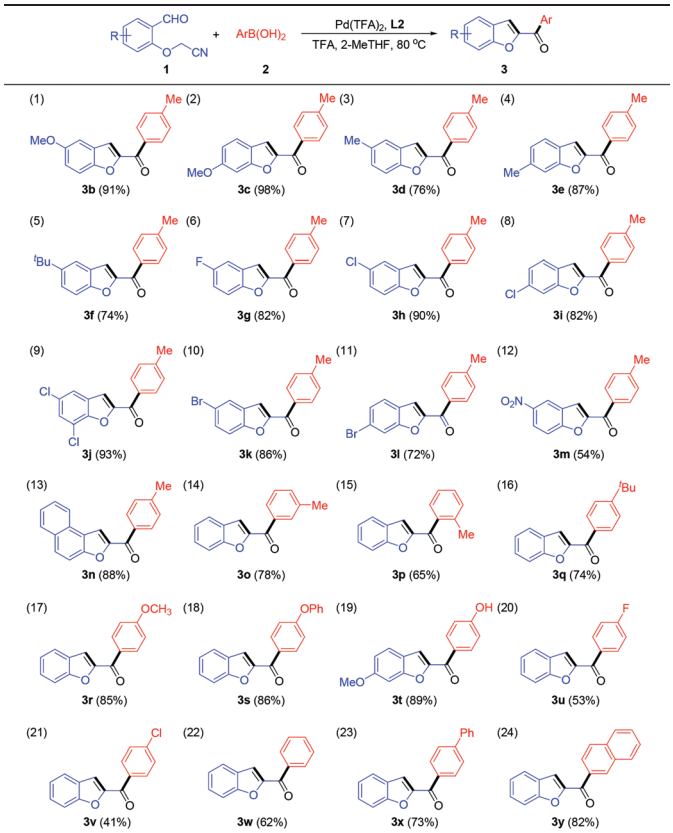
Table 1 Optimization of reaction conditions[a]



Entry	[Pd]	Ligand	Additive	Solvent	Yield[b] (%)
1	$PdCl_2$	**L1**	TFA	THF	Trace
2	$Pd(PPh_3)_4$	**L1**	TFA	THF	13
3	$Pd(OAc)_2$	**L1**	TFA	THF	45
4	$Pd(dba)_2$	**L1**	TFA	THF	51
5	$Pd(acac)_2$	**L1**	TFA	THF	58
6	$Pd(TFA)_2$	**L1**	TFA	THF	62
7	$Pd(TFA)_2$	**L2**	TFA	THF	84
8	$Pd(TFA)_2$	**L3**	TFA	THF	48
9	$Pd(TFA)_2$	**L4**	TFA	THF	55
10	$Pd(TFA)_2$	**L5**	TFA	THF	53
11	$Pd(TFA)_2$	**L6**	TFA	THF	49
12	$Pd(TFA)_2$	**L7**	TFA	THF	71
13	$Pd(TFA)_2$	**L8**	TFA	THF	74
14	$Pd(TFA)_2$	**L9**	TFA	THF	56
15	$Pd(TFA)_2$	**L10**	TFA	THF	22
16	$Pd(TFA)_2$	**L2**	TsOH H_2O	THF	35
17	$Pd(TFA)_2$	**L2**	CF_3SO_3H	THF	11
18	$Pd(TFA)_2$	**L2**	CH_3CO_2H	THF	31
19	$Pd(TFA)_2$	**L2**	$PhCO_2H$	THF	24
20	$Pd(TFA)_2$	**L2**	HCl	THF	0
21	$Pd(TFA)_2$	**L2**	$ZnCl_2$	THF	0
22	$Pd(TFA)_2$	**L2**	TFA	Toluene	43
23	$Pd(TFA)_2$	**L2**	TFA	1,4-Dioxane	74
24	$Pd(TFA)_2$	**L2**	TFA	DMF	73
25	$Pd(TFA)_2$	**L2**	TFA	EtOH	37
26	$Pd(TFA)_2$	**L2**	TFA	H_2O	46
27	$Pd(TFA)_2$	**L2**	TFA	2-MeTHF	92
28		**L2**	TFA	2-MeTHF	0
29	$Pd(TFA)_2$		TFA	2-MeTHF	0

[a] Conditions: **1a** (0.4 mmol), **2a** (0.8 mmol), Pd catalyst (5 mol%), ligand (10 mol%), additive (10 equiv.), solvent (2 mL), 80 °C, 24 h, air. [b] Isolated yield.

Table 2 Synthesis of 2-aroyl benzofurans[a]

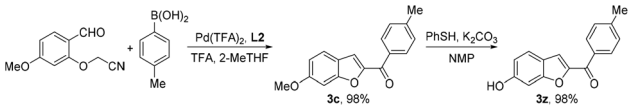


[a] Conditions: **1** (0.4 mmol), **2** (0.8 mmol), $Pd(TFA)_2$ (5 mol%), **L2** (10 mol%), TFA (10 equiv.), 2-MeTHF (2 mL), 80 °C, 24 h, air, isolated yield.

2-(2-formylphenoxy)acetonitrile derivatives undergo tandem addition/cyclization with *p*-tolylboronic acid (**2a**) efficiently, thus including electron-rich methoxy, methyl and *tert*-butyl substituents (**3b–3f**). Moreover, halogen-substituted (*e.g.*, –F, –Cl, –Br) substrates were well tolerated (**3g–3l**). However, substrate bearing a strongly electron-withdrawing group (*e.g.*, $–NO_2$) decreased the yield of **3m** to 54% (entry 12). Notably, treatment of 2-((1-formylnaphthalen-2-yl)oxy)acetonitrile with **2a** also proceeded smoothly and gave the desired product **3n** in 88% yield (entry 13). We were delighted to find that this newly developed protocol to be compatible with a wide variety of arylboronic acids. Functional groups, including electron-donating groups such as methyl (**3o–3p**), *tert*-butyl (**3q**), methoxy (**3r**), phenoxy (**3s**) and hydroxyl (**3t**) and electron-withdrawing groups such as fluoro (**3u**) and chloro (**3v**), were well tolerated. Polyaromatic substrates, such as biphenyl-4-ylboronic acid and naphthalen-2-ylboronic acid, were also good partners and coupled with **1a** efficiently, affording the corresponding products **3x** and **3y** in good yields (entries 23 and 24). It is worth noting that the products derived from 2-(2-formylphenoxy)acetonitriles bearing bromo and hydroxyl groups (**3k**, **3l**, **3t**) leave intact synthetic handles for further synthetic elaborations thereby broadening the molecular diversity. However, we attempted to perform this tandem reaction of 2-(2-formylphenoxy)acetonitrile (**1a**) with alkylboronic acids (*e.g.* benzylboronic acid, methylboronic acid, cyclopropylboronic acid) under the standard conditions failed to give the desired products.

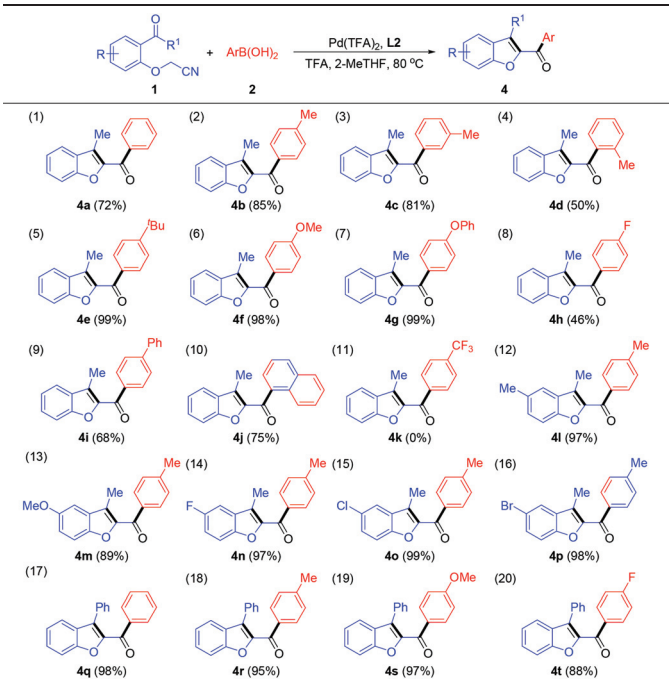
In addition, transformation of (6-methoxybenzofuran-2-yl)(*p*-tolyl)methanone (**3c**) as a representative example is shown in Scheme 2, providing the corresponding (6-hydroxybenzofuran-2-yl)(*p*-tolyl)methanone (**3z**).

We next turned our attention to the scope of this reaction with respect to the 2-(2-acylphenoxy)acetonitriles (Table 3). First, reaction of 2-(2-acetylphenoxy)acetonitrile (**1b**) with arylboronic acids was examined. Treatment of **1b** with phenylboronic acid gave the desired product (3-methylbenzofuran-2-yl)(phenyl)methanone (**4a**) in 72% yield (entry 1). The reactivities of *para*-, *meta*-, and *ortho*-tolylboronic acids were evaluated, and the results demonstrated that the steric effect of substituent had an obvious impact on the reaction. For example, treatment of **1b** with *para*-, and *meta*-tolylboronic acids provided 85% and 81% yields of **4b** and **4c**, respectively (entries 2



Scheme 2 Transformation of **3c**.

Table 3 Synthesis of 3-substituted 2-aroyl benzofurans[a]



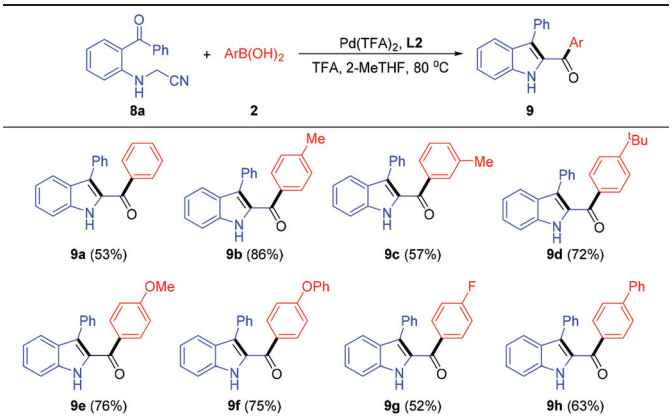
[a] Conditions: **1** (0.4 mmol), **2** (0.8 mmol), $Pd(TFA)_2$ (5 mol%), **L2** (10 mol%), TFA (10 equiv.), 2-MeTHF (2 mL), 80 °C, 24 h, air, isolated yield.

and 3), while the *ortho*-tolylboronic acid afforded the desired product **4d** in 50% yield (entry 4). Other electron-donating groups, *tert*-butyl, methoxy and phenoxy, were well tolerated and afforded the corresponding products **4e–4f** in excellent yields (entries 5–7). The reaction of fluoro-, phenyl- and naphthyl-substituted arylboronic acids with **1b** afforded the corresponding products **4g–4j** in acceptable yields (entries 8–10). However, the reaction failed to afford the desired product **4k** when substrate bearing the strong electron-withdrawing CF_3 group was used (entry 11). The reaction of methyl-, methoxy-, and halogen-substituted substrates with *p*-tolylboronic acid (**2a**) also proceeded smoothly and gave the desired products **4l–4p** in good to excellent yields (entries 12–16). Of significant interest is the bromo-substituted product **4p**, which could be amenable to further functionalization. Reaction of 2-(2-benzoylphenoxy)acetonitrile (**1c**) with phenylboronic acid gave the desired product **4q** in 98% yield (entry 17). An investigation of the reaction of other arylboronic acids with **1c** revealed that both electron-rich (*e.g.*, –Me, –OMe) and electron-deficient (*e.g.*, –F) substituents were tolerated and the desired products **4r–4t** were obtained in 88–97% yield (entries 18–20).

Then, the utility of this methodology was further applied to the synthesis of 1-(benzofuran-2-yl(phenyl)methyl)-1*H*-1,2,4-triazole, which was the representative compound identified as the potent CYP19 inhibitor.[12b] As shown in Scheme 3, the key intermediate (4-fluorophenyl)(6-methoxybenzofuran-2-yl) methanone (**5a**) was obtained in moderate yield by the treatment of the readily available 2-(2-formyl-5-methoxyphenoxy) acetonitrile (**1d**) with (4-fluorophenyl)boronic acid (**2b**). Next, sodium borohydride reduction of **5a** gave (4-fluorophenyl)(6-methoxybenzofuran-2-yl)methanol (**6a**) in 91% yield, which was converted into the target triazole **7a** in 79% yield in the presence of triazole and thionyl chloride. Compared with other synthetic procedures, this process was easy to handle with commercially available starting materials.

This methodology has also been applied to the synthesis of 2-aroyl indoles from the tandem addition/cyclization of 2-((2-benzoylphenyl)amino)acetonitrile (**8a**) with arylboronic acids (Table 4). Treatment of **8a** with phenylboronic acid gave the desired product phenyl(3-phenyl-1*H*-indol-2-yl)methanone (**9a**) in 53% yield (entry 1). The electronic properties of the substituents on the phenyl ring of the arylboronic acids affected the yields of the reaction to some extent. Not only electron-donating groups, such as methyl (**9b–9c**), *tert*-butyl (**9d**), methoxy (**9e**) and phenoxy (**9e**) but also electron-withdrawing groups, such as fluoro (**9g**) and phenyl (**9h**) on the phenyl ring of arylboronic acids, were tolerated in this transformation.

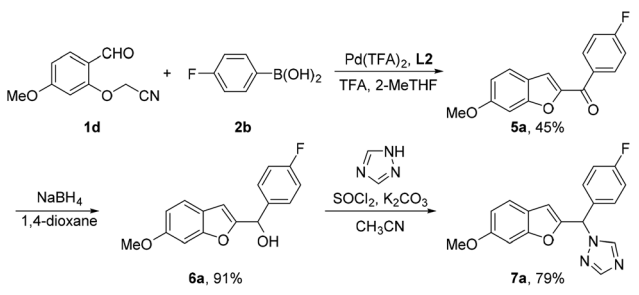
Table 4 Synthesis of 2-aroyl indoles[a]



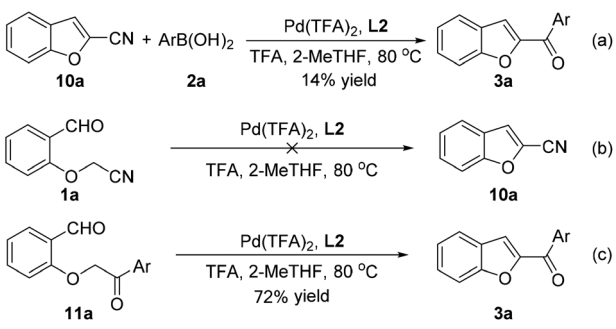
[a] Conditions: **8a** (0.4 mmol), **2** (1.2 mmol), $Pd(TFA)_2$ (5 mol%), **L2** (10 mol%), TFA (10 equiv.), 2-MeTHF (2 mL), 80 °C, 24 h, air, isolated yield.

To gain insight into the reaction mechanism, further experimental studies were performed (Scheme 4). Treatment of benzofuran-2-carbonitrile (**10a**) with *p*-tolylboronic acid (**2a**) deliver benzofuran-2-yl(*p*-tolyl)methanone (**3a**) in 14% yield (Scheme 4a). However, we attempted to perform the reaction in the absence of arylboronic acid under the standard conditions failed to give **10a** (Scheme 4b). We found that the desired product **3a** was obtained in 72% yield when 2-(2-oxo-2-(*p*-tolyl)ethoxy)benzaldehyde (**11a**) was used (Scheme 4c). These results indicated that **11a** was proposed as a possible intermediate for this transformation.

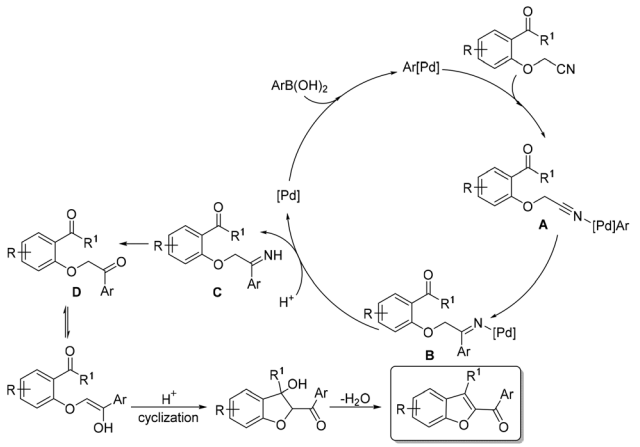
On the basis of the above-mentioned results, a possible mechanism for the formation of 2-aroyl benzofurans is shown in Scheme 5. Transmetallation of the palladium species with $ArB(OH)_2$ to give Ar[Pd], which was followed by the coordination of 2-(2-acylphenoxy)acetonitriles to produce intermedi-



Scheme 3 Synthesis of the potent CYP19 inhibitor.



Scheme 4 Control experiments (Ar = *p*-MeC_6H_4).



Scheme 5 Plausible reaction mechanism.

ate **A**. Next, carbopalladation of the cyano group gave imine intermediate **B**. In the presence of TFA, protonation of the intermediate **B** would afford intermediate **C** and regenerates palladium catalyst. Hydrolysis of the intermediate **C** would deliver ketone **D**. Finally, keto–enol tautomerism and a subsequent cyclization/dehydration under acidic conditions would afford the corresponding 2-aroyl benzofurans as the desired products.

Conclusions

In summary, we have developed a new strategy for the synthesis of structurally diverse 2-aroyl benzofurans in moderate to excellent yields by the Pd-catalyzed tandem addition/cyclization of 2-(2-acylphenoxy)acetonitriles with arylboronic acids. This system shows remarkable chemoselectivity and broad substrate scope. In addition, this protocol also applies to the synthesis of 2-aroyl indoles and the potent CYP19 inhibitor 1-(benzofuran-2-yl(phenyl)methyl)-1*H*-1,2,4-triazole.

Experimental section

General methods

Melting points are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were measured on a 500 MHz or 400 MHz spectrometer using $CDCl_3$ as the solvent with tetramethylsilane (TMS) as an internal standard at room temperature. Chemical shifts are given *n* δ relative to TMS, and the coupling constants *J* are given in hertz. High-resolution mass spectra were recorded on an ESI-Q-TOF mass spectrometer. The starting materials 2-(2-formylphenoxy)acetonitriles (**1**),[17] 2-(2-acetylphenoxy) acetonitrile (**1b**),[18] 2-(2-benzoylphenoxy)acetonitrile (**1c**)[19] and 2-(2-oxo-2-(*p*-tolyl)ethoxy) benzaldehyde (**11a**)[20] were synthesized according to the method described in the literature. Column chromatography was performed using EM silica gel 60 (300–400 mesh).

Typical procedure for the synthesis of 8a

A mixture of (2-hydroxyphenyl)(phenyl)methanone (198 mg, 1 mmol), bromoacetonitrile (144 mg, 1.2 mmol), potassium carbonate (165 mg, 1.2 mmol) and DMF (15 mL) was stirred at 60 °C for 24 h. The progress of the reaction was monitored using TLC. After the completion of the reaction, the reaction mixture was diluted with ethyl acetate (50 mL), washed with water (3 × 100 mL), brine (2 × 10 mL), and dried over anhydrous Na_2SO_4. The residue was purified by flash column chromatography (hexane/ethyl acetate) to afford 2-((2-benzoylphenyl)amino)acetonitrile (**8a**).

2-((2-Benzoylphenyl)amino)acetonitrile (8a). Pale-yellow oil (127 mg, 54%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.66 (s, 1H), 7.63–7.46 (m, 7H), 6.88 (d, *J* = 8.0 Hz, 1H), 6.78 (t, *J* = 8.0 Hz, 1H), 4.26 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 199.7, 148.9, 139.7, 135.6, 135.2, 131.1, 129.2, 128.2, 119.4, 116.8, 116.3, 111.5, 31.4. HRMS calcd for $C_{15}H_{13}N_2O$ $[M + H]^+$: 237.1023, found 237.1024.

General procedure for the synthesis of 2-aroyl benzofurans or 2-aroyl indoles

Arylboronic acid, 2-(2-acylphenoxy)acetonitrile or 2-((2-benzoylphenyl)amino)acetonitrile, $Pd(TFA)_2$, 6,6′-dimethyl-2,2′-bipyridine **L2**, TFA and 2-MeTHF were successively added into a Schlenk reaction tube under air. The reaction mixture was stirred for 10 minutes at room temperature for proper mixing of the reactants, and then heated at 80 °C with vigorous stirring for 24 hours. After the reaction equilibrium, the mixture was poured into ethyl acetate, which was washed with saturated $NaHCO_3$ (2 × 10 mL) and then brine (10 mL). After the aqueous layer was extracted with ethyl acetate, the combined organic layers were dried over anhydrous Na_2SO_4 and evaporated under a vacuum. The residue was purified by flash column chromatography (hexane/ethyl acetate) to afford 2-aroyl benzofurans or 2-aroyl indoles.

(5-(*tert*-Butyl)benzofuran-2-yl)(*p*-tolyl)methanone (3f). Yellow oil (86.6 mg, 74%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 8.4 Hz, 2H), 7.70 (s, 1H), 7.56 (d, *J* = 1.6 Hz, 2H), 7.49 (s, 1H), 7.32 (d, *J* = 8.0 Hz, 2H), 2.45 (s, 3H), 1.39 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 184.0, 154.3, 152.7, 147.1, 143.7, 134.7, 129.7, 129.2, 126.8, 126.6, 119.0, 116.3, 111.9, 34.8, 31.7, 21.7. HRMS (ESI) calcd for $C_{20}H_{20}O_2Na$ $[M + Na]^+$: 315.1361, found 315.1355.

(4-(*tert*-Butyl)phenyl)(3-methylbenzofuran-2-yl)methanone (4e). Yellow oil (115.7 mg, 99%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.14–8.11 (m, 2H), 7.71–7.69 (m, 1H), 7.59–7.55 (m, 3H), 7.51–7.46 (m, 1H), 7.36–7.32 (m, 1H), 2.68 (s, 3H), 1.41 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 185.4, 156.3, 154.3, 148.6, 135.2, 129.8, 129.3, 128.0, 126.4, 125.3, 123.3, 121.4, 112.2, 35.1, 31.2, 10.0. HRMS (ESI) calcd for $C_{20}H_{20}O_2Na$ $[M + Na]^+$: 315.1361, found 315.1356.

(4-Fluorophenyl)(3-phenylbenzofuran-2-yl)methanone (4t). Pale-yellow solid (111.3 mg, 88%), mp 143–144 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95–7.92 (m, 2H), 7.72 (d, *J* = 8.0 Hz, 1H), 7.65 (d, *J* = 8.5 Hz, 1H), 7.56–7.49 (m, 3H), 7.41–7.35 (m, 4H)

7.03 (t, J = 7.5 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 184.1, 165.6 (d, J = 252.5 Hz), 154.6, 147.0, 133.6, 133.5, 132.5 (d, J = 8.8 Hz), 130.9, 130.0, 129.6, 128.5, 128.4, 128.1, 124.1, 122.4, 115.3 (d, J = 22.5 Hz), 112.4. HRMS (ESI) calcd for $C_{21}H_{13}FO_2Na$ $[M + Na]^+$: 339.0798, found 339.0804.

3-Phenyl-1*H*-indol-2-yl(*m*-tolyl)methanone (9c). Pale-yellow solid (70.9 mg, 57%), mp 122–123 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.68 (s, 1H), 7.68 (d, J = 8.0 Hz, 1H), 7.47 (d, J = 8.0 Hz, 1H), 7.38–7.34 (m, 2H), 7.19–7.08 (m, 7H), 7.03–6.96 (m, 2H), 2.03 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 189.9, 137.4, 137.3, 136.5, 134.0, 132.5, 131.1, 130.8, 130.7, 127.9, 127.8, 127.7, 126.8, 126.6, 125.4, 122.1, 121.1, 112.1, 20.9. HRMS calcd for $C_{22}H_{17}NONa$ $[M + Na]^+$: 334.1208, found 334.1220.

(4-(*tert*-Butyl)phenyl)(3-phenyl-1*H*-indol-2-yl)methanone (9d). Pale-yellow solid (101.7 mg, 72%), mp 199–200 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.39 (s, 1H), 7.73 (d, J = 8.0 Hz, 1H), 7.51 (d, J = 8.0 Hz, 1H), 7.44–7.40 (m, 3H), 7.20 (m, 3H), 7.11–7.05 (m, 5H), 1.22 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 189.5, 155.2, 136.4, 134.7, 133.9, 131.2, 130.9, 129.4, 127.9, 127.8, 126.6, 126.5, 125.4, 124.5, 122.2, 121.1, 112.0, 34.8, 31.0. HRMS (ESI) calcd for $C_{25}H_{24}NO$ $[M + H]^+$: 354.1853, found 354.1860.

(4-Phenoxyphenyl)(3-phenyl-1*H*-indol-2-yl)methanone (9f). White solid (116.7 mg, 75%), mp 179–180 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.35 (s, 1H), 7.74 (d, J = 8.0 Hz, 2H), 7.54–7.51 (m, 3H), 7.42 (d, J = 8.0 Hz, 1H), 7.36 (d, J = 8.0 Hz, 2H), 7.22–7.14 (m, 7H), 6.91 (d, J = 8.5 Hz, 2H), 7.66 (d, J = 8.5 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 188.3, 160.5, 156.2, 136.3, 134.3, 134.0, 132.4, 131.8, 131.0, 129.8, 128.1, 127.7, 126.8, 126.5, 124.9, 124.0, 122.0, 121.2, 119.4, 117.3, 112.0. HRMS (ESI) calcd for $C_{27}H_{20}NO_2$ $[M + H]^+$: 390.1489, found 390.1484.

(4-Fluorophenyl)(3-phenyl-1*H*-indol-2-yl)methanone (9g). Pale-yellow solid (65.5 mg, 52%), mp 144–145 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.55 (s, 1H), 7.74 (d, J = 8.0 Hz, 1H), 7.57–7.51 (m, 3H), 7.42 (t, J = 7.5 Hz, 1H), 7.21–7.17 (m, 6H), 6.74 (t, J = 8.5 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 188.2, 165.8, 163.8, 136.6, 133.8, 133.7, 132.1, 132.0, 130.9, 130.8, 128.1, 126.9, 127.6, 127.1, 126.7, 125.4, 122.1, 121.3, 114.8, 114.6, 112.1. HRMS (ESI) calcd for $C_{21}H_{14}FNONa$ $[M + Na]^+$: 338.0957, found 338.0956.

[1,1′-Biphenyl]-4-yl(3-phenyl-1*H*-indol-2-yl)methanone (9h). Pale-yellow solid (94.0 mg, 63%), mp 144–145 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.70 (s, 1H), 7.74 (d, J = 8.0 Hz, 2H), 7.53 (d, J = 8.0 Hz, 1H), 7.47–7.34 (m, 6H), 7.28–7.26 (m, 2H), 7.22–7.17 (m, 3H), 7.12–7.11 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 189.2, 144.3, 140.3, 136.6, 136.4, 133.9, 131.2, 131.0, 130.1, 128.8, 128.0, 127.9, 127.8, 127.2, 126.8, 126.6, 126.3, 125.4, 122.2, 121.2. HRMS (ESI) calcd for $C_{21}H_{14}FNONa$ $[M + Na]^+$: 396.1365, found 396.1371.

Conflicts of interest

There are no conflicts of interest to declare.

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