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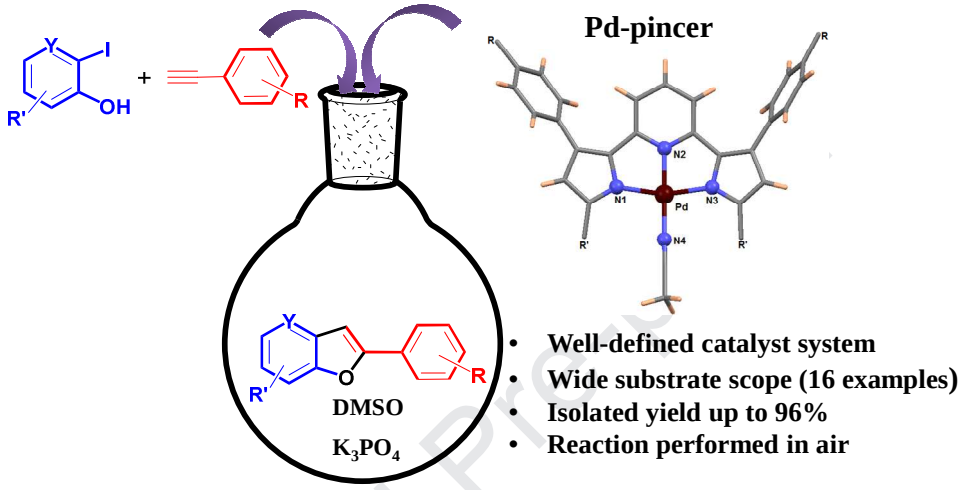
Graphical Abstract:

Bis(pyrrolyl)pyridine based palladium-pincer complexes efficiently catalyzed the one-pot tandem Heck alkynylation/cyclization reactions for the synthesis of benzofuran derivatives.



One-Pot Tandem Heck Alkynylation/Cyclization Reactions Catalyzed by Bis(Pyrrolyl)pyridine based Palladium Pincer Complexes

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Abstract:

Ligand assisted palladium catalyzed one-pot tandem Heck alkynylation/cyclization reactions for the synthesis of benzofurans was reported in this paper. Well-defined palladium-pincer complexes exhibited excellent catalytic activities for the one-pot tandem Heck alkynylation/cyclization reactions yielding benzofuran derivatives using 0.1 mol% catalyst. All the catalytic reactions are performed in air. The effects of variables such as solvents, the temperature on the catalytic activity are also reported. High product conversion was obtained for differently substituted 2-iodophenol at 120 ^{o}C in 10 hours.

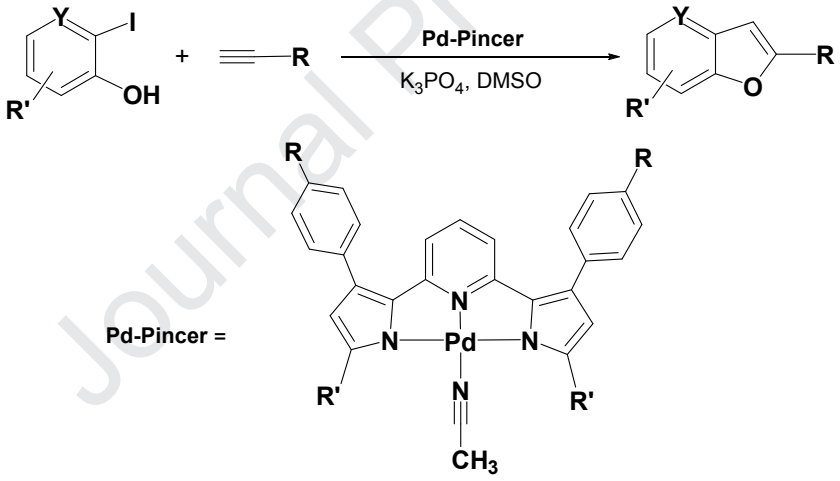
Keywords: Bis(pyrrolyl)pyridine, Palladium, Heck alkynylation, tandem reaction, Benzofurans

1. INTRODUCTION

Heterocyclic compounds are present in many natural products and medicinal chemistry.[1] A large number of oxygen containing heterocyclic compounds are known for their versatility and unique properties in many chemotherapeutic agents and also exhibit excellent antibiotic activity.[2] Benzofuran is the one of these heterocyclic compounds are found in many natural, pharmaceutical products as well as in polymers.[3] Many traditional methods are available for the synthesis of benzofuran derivatives which involve multistep reactions with low functional group tolerance.[4] Tandem approach are becoming increasingly popular and beginning to get attention due to environmentally benign and time improvement methodology.[5] Tandem Heck alkynylation/cyclization reaction (also known as domino Sonogashira coupling/cyclization) catalyzed by transition metal catalysts has emerged as an efficient and powerful method.[6] Tandem Heck alkynylation/cyclization reaction required combination of palladium and copper catalysts. However, few examples of copper-free palladium catalyzed tandem Heck alkynylation/cyclization reaction for the synthesis of benzofuran derivatives are reported in the literature.[7,8,9] Some of the palladium catalyzed tandem processes are also reported with high catalyst loading. Therefore, a highly efficient, well-defined catalytic system is of considerable importance.

Ligands play an important role in homogeneous transition metal-catalyzed reactions for the efficient synthesis of biologically important scaffolds.[10] The ligand framework in the transition metal complexes regulates both the electronic and steric properties, which in turn significantly affects their catalytic performance. Pincer ligands are an important class of ligands in metal-based catalytic reactions for the synthesis of heterocycles in an efficient manner. Transition

metal complexes with 2,6-bis(pyrrolyl)pyridine ligand framework were not much studied in homogeneous catalysis. The ligand framework has been used for the isolation of reaction intermediate,[11] LMCT photosensitizers,[12] and in catalytic processes.[12] Recently, we have reported a series of bis(pyrrolyl)pyridine ligand-based palladium catalysts for Suzuki-Miyaura cross-coupling reactions in aqueous medium.[13] After we observed its potential in the catalytic transformation, we became interested to utilize these classes of palladium pincer complexes (**2a**-**2b**, Scheme 1) for the synthesis of benzofuran derivatives using tandem Heck alkynylation reaction and intramolecular cyclization strategy. To our best of knowledge, this work is the first successful application of 2,6-bis(pyrrolyl)pyridine pincer ligand based palladium catalysts for one-pot tandem Heck alkynylation/cyclization reaction at low catalyst loading (Scheme 1).

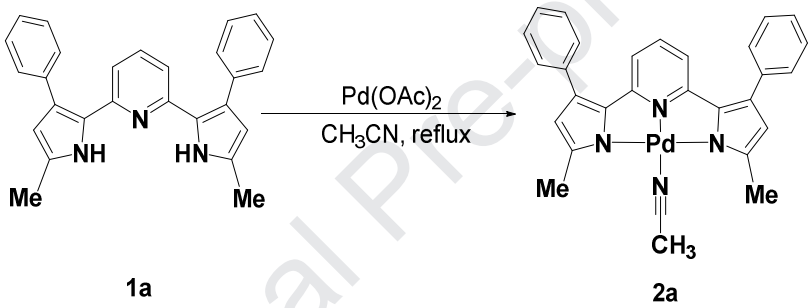


Scheme 1. Palladium-pincer complexes catalyzed one-pot tandem Heck alkynylation/cyclization reactions

2. Results and Discussion

2.1. Synthesis and characterization of palladium complexes

The palladium complex **2a** was synthesized from the reaction of corresponding ligand **1a** and $Pd(OAc)_2$ in acetonitrile as shown in Scheme 2. The palladium complex **2a** was characterized by NMR spectroscopy, elemental analysis, and Mass spectrometry. The formation of **2a** is confirmed by ^1H NMR spectroscopy through observing the disappearance of the pyrrole proton signal at 9.59 ppm in ligand **1a**,[12] which indicates the formation of the Pd-$N_{pyrrole}$ bond. The HR-MS data of the complex **2a** exhibit the molecular ion peak *m*/*z* 535.1114 corresponding to the molecular formula of the palladium complex. The palladium complex **2b** was reported earlier from our group.[13]



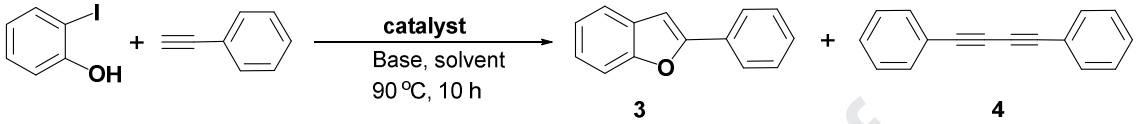
Scheme 2. Synthesis of palladium-pincer complex **2a**.

2.2. One-pot tandem Heck alkynylation/cyclization reaction

In the first step of our catalytic studies, we selected the coupling of 2-iodophenol and phenylacetylene as model substrates. To optimize the reaction conditions, various solvents (entries 3-7) and bases (entries 1-3) were tested using **2b** as a catalyst. Similar to earlier studies, the base K_3PO_4 and solvent DMSO provided the best condition (entry 3) at 90° C for complete conversion with 0.0005 mmol (0.1 mol %) catalyst loading in 10 hours in air. In some cases, the cyclized product **3** was obtained along with a by-product **4** (Glaser coupling)[14] as shown in Table 1. On comparison, the reaction in the presence of palladium precursor *i.e.* $PdCl_2(CH_3CN)_2$ gave

48% conversion in the same reaction conditions (entry 9). Reactions performed without palladium sources did not yield the expected benzofuran product (entry 10).

Table 1. Optimization of the reaction conditions for synthesis of 2-arylbenzofuran[a]



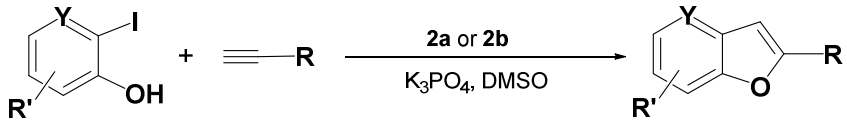
3 4

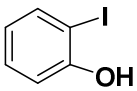
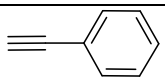
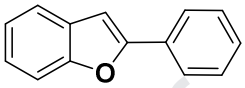
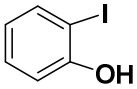
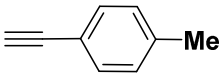
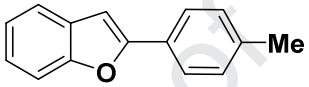
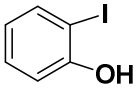
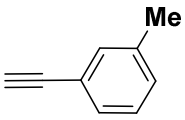
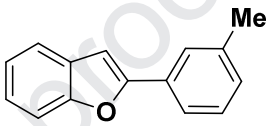
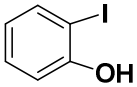
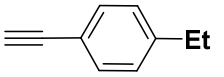
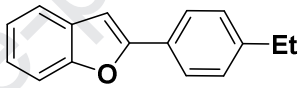
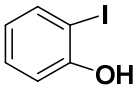
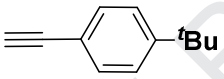
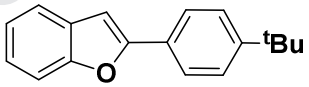
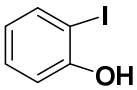
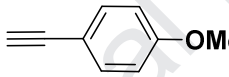
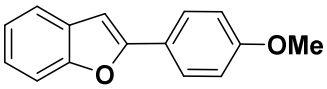
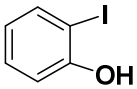
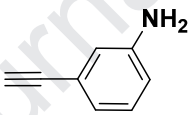
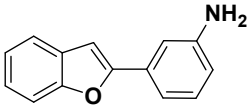
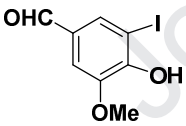
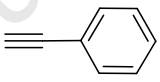
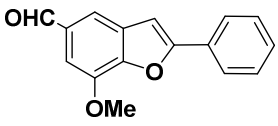
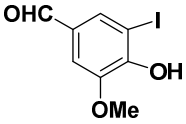
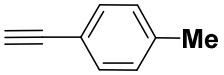
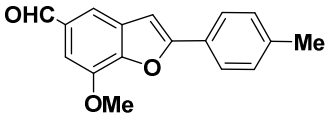
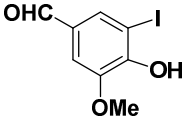
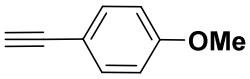
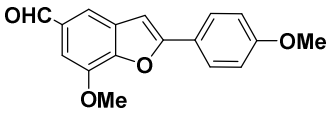
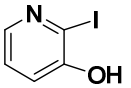
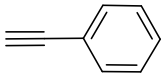
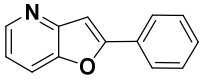
Entry	Catalyst Loading (mol %)	Solvent	Base	% Yield[b]	
				3	**4**
1.	**2b** (0.1)	DMSO	Et_3N	32	51
2.	**2b** (0.1)	DMSO	Cs_2CO_3	15	7
3.	**2b** (0.1)	**DMSO**	**K_3PO_4**	**>99(96)[c]**	-
4.	**2b** (0.1)	DMF	K_3PO_4	86	0
5.	**2b** (0.1)	1,4-Dioxane	K_3PO_4	22	10
6.	**2b** (0.1)	EtOH	K_3PO_4	trace	-
7.	**2b** (0.1)	toluene	K_3PO_4	29	46
8.	**2b** (0.1)	DMSO	-	11	-
9.	$PdCl_2(CH_3CN)_2$ (0.1)	DMSO	K_3PO_4	48	-
10.	-	DMSO	K_3PO_4	nr[d]	nr

[a]Reaction conditions: 2-Iodophenol (0.50 mmol), phenylacetylene (0.60 mmol), 0.1 mol % (0.0005 mmol) of catalyst, base (1.00 mmol), and solvent (2 mL). [b]The yields (%) were determined by GC using 1,3,5-trimethoxybenzene as an internal standard. [c]Isolated yield. [d]Without catalyst. nr = No reaction.

Considering the highest conversion of the product in DMSO using K_3PO_4 as a base (entry 3, Table 1), several commercially available substituted 2-iodophenol and terminal alkynes (with electron-withdrawing/donating group and amine group) have been tested in the same reaction conditions. All the catalysis products were characterized by NMR, and compared with literature data. The iodophenol based substrates such as 5-iodovanillin and 2-iodo-3-hydroxypyridine gave low reaction yields (21-31%) using identical condition at 90 ^{o}C. We observe the lowest yields, up to 18% for the reaction of propargyl alcohol with and 2-iodophenol.

Table 2. One-pot tandem Heck alkynylation/cyclization reactions by **2a** and **2b** at 90 °C.[a]



S.No.	Iodophenol	Alkyne	Product	Yield (%)[b]	
				2a	**2b**
1.				89	96
2.				88	90
3.				81	73
4.				79	84
5.				65	69
6.				82	86
7.				39	46
8.				26	31
9.				25	28
10.				23	27
11.				21	24

[a]Reaction conditions: 2-Iodophenol (0.50 mmol), alkyne (0.60 mmol), 0.1 mol % of **2a** or **2b**, K_3PO_4 (1.00 mmol), DMSO (2 mL), 90 °C, 10 hours. [b]Isolated yield.

The effect of temperature on the reaction rate was studied for one-pot tandem Heck alkynylation/cyclization reactions. The reactions are performed using the substrates 5-iodovanillin and 4-ethynyltoluene in the presence of catalyst **2b** at five different temperatures from 80-120 ^{o}C (Figure 1). The reaction rate was increased exponentially on increasing the reaction temperature from 80 ^{o}C to 120 ^{o}C. The reaction of 5-iodovanillin with 4-ethynyltoluene at 80 ^{o}C gave only 26% product conversion, whereas, on raising the reaction temperature to 120 ^{o}C resulted in enhancement of product conversion up to 83% in same reaction time.

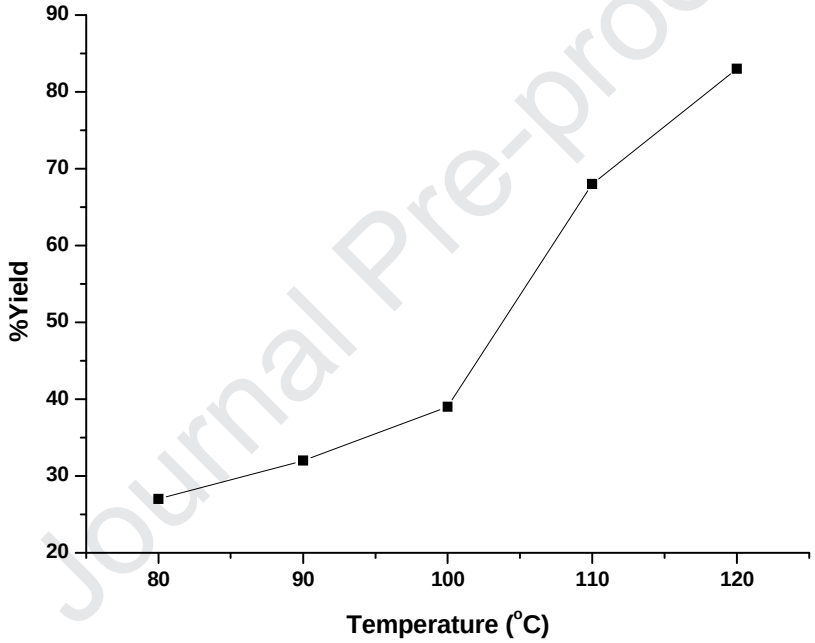
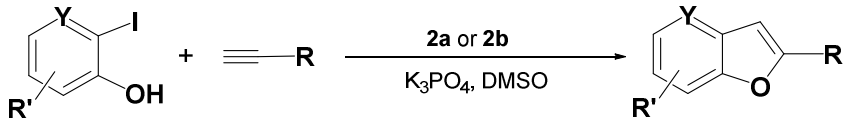
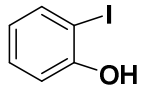
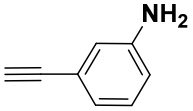
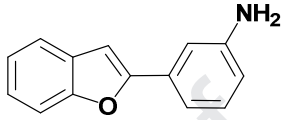
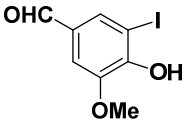
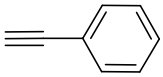
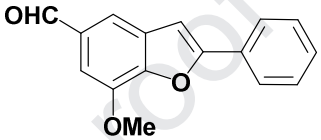
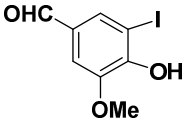
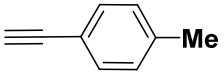
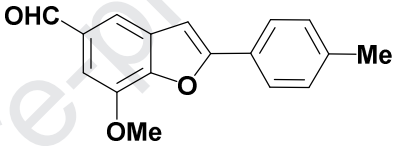
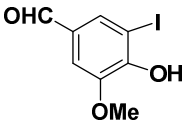
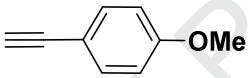
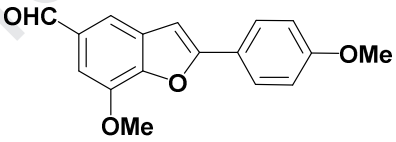
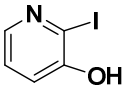
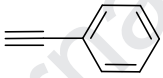
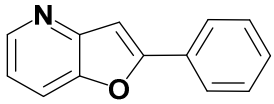
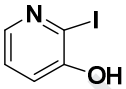
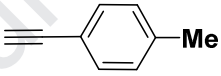
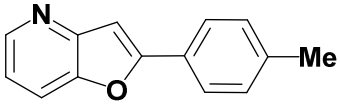
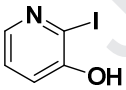
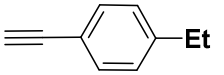
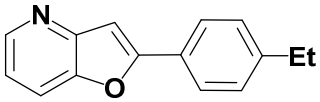
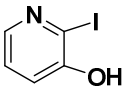
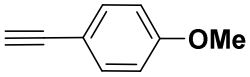
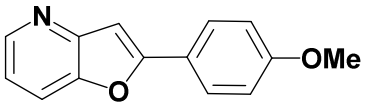
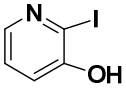
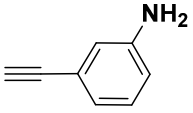
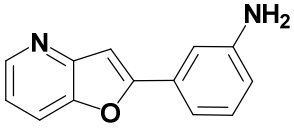
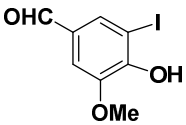
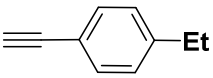
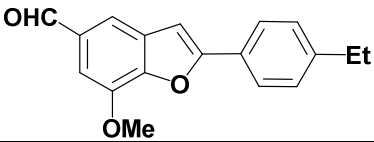


Figure 1. Effect of temperature on reaction rate for one-pot tandem Heck alkynylation/cyclization reaction (5-iodovanillin with 4-ethynyltoluene)

The yields of the benzofuran derivatives at temperature 120 ^{o}C in 10 hours of reaction time are shown in Table 3. The yields were increased up to 83% in the case of 5-iodovanillin, whereas 2-iodo-3-hydroxypyridine substrate gave only up to 63%. When the catalyst loading was decreased to 0.05 mol % at 120 ^{o}C for the reaction of 2-iodophenol with phenylacetylene, only 62% product conversion was observed after 10 hours.

Table 3. One-pot tandem Heck alkynylation/cyclization reactions by **2a** and **2b** at 120 °C.[a]



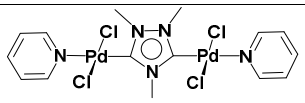
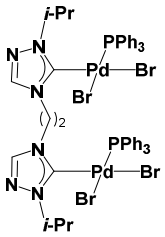
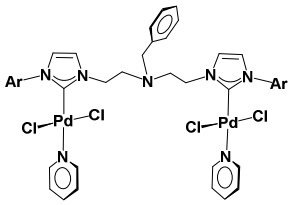
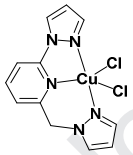
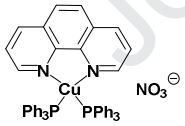
S.No.	Iodophenol	Alkyne	Product	Yield (%)[b]	
				2a	**2b**
12.				83	84
13.				74	79
14.				78	83
15.				70	78
16.				58	63
17.				52	58
18.				51	56
19.				53	62
20.				56	53
21.				85	86

[a]Reaction conditions: 2-Iodophenol derivatives (0.50 mmol), alkyne (0.60 mmol), 0.1 mol % of **2a** or **2b**, K_3PO_4 (1.00 mmol), DMSO (2 mL), 120 °C, 10 hours. [b]Isolated yield.

The comparison of the catalytic efficiencies of **2a** and **2b** complexes with other reported well-defined palladium based catalysts for one-pot tandem Heck alkynylation/cyclization reactions yielding benzofuran compounds is important (Table 4). Peris and co-workers reported initially the one-pot tandem Heck alkynylation/cyclization reaction of 2-iodophenol with phenylacetylene, yielding 2-phenylbenzofuran by using 1 mol % N-heterocyclic carbene based palladium catalysts.[9c] Ghosh and co-workers reported the same catalytic transformation with 1 mol % of palladium catalyst supported by N-heterocyclic carbene and phosphine based ligands.[9a] Recently, we have reported the same one-pot tandem Heck alkynylation/cyclization reactions with 0.2 mol % of N-heterocyclic carbene-palladium catalysts.[9b] In addition to this, few well-defined copper(II) complexes also catalyzed the tandem reaction of 2-iodophenol with various terminal alkynes.[6b,15] Concerning the examples from the *in situ* generated ligand assisted catalysis systems with a phosphine based ligand (0.1 mol %) and palladium precursor $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ (0.05 mol %) catalyzed the reaction with excellent yield.[8a] Thus, in comparison to the above reported well-defined catalysts, the palladium pincer complexes **2a**–**2b** is efficient at 0.1 mol % catalyst loading and also has wide substrate scope (Table 4).

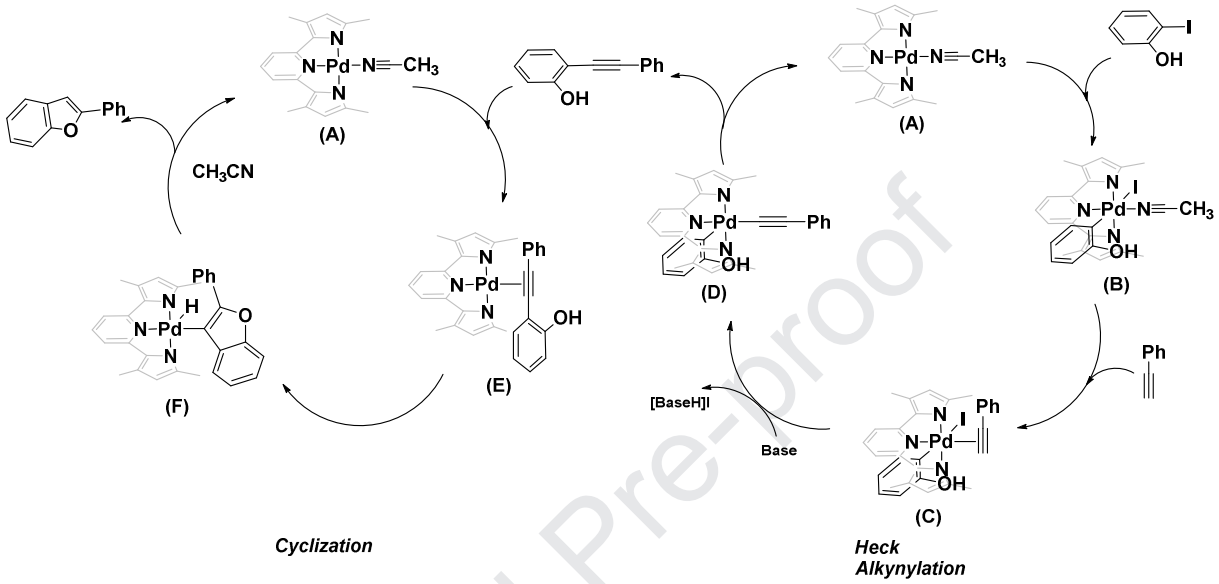
Based on our results and previous reports,[8a,9a] the possible reaction mechansim for the generation of benzofuran derivatives was proposed in Scheme 3. The mechanism involves two catalytic cycles, the Heck alkynylation cycle and an intramolecular cyclization reaction. Since our pincer based catalysts are stable in catalytic reaction temperature,[13] the first catalytic cycle may initiates *via* Pd(II)/Pd(IV) catalytic reactions[16] instead of Pd(0)/Pd(II) chemistry, the oxidative addition of Pd(II) complexes with 2-iodophenol yields a Pd(IV) intermdediate (**B**). The coordination of phenylacetylene to palladium by elimination solvent molecule yielded the intermediate **C**.

Table 4. Comparison with reported transition metal well-defined catalysts for one-pot tandem Heck alkynylation/cyclization reaction of 2-iodophenol with phenylacetylene, giving 2-phenylbenzofuran.

No.	catalyst	loading (mol %)	time (h)	base/ solvent	Temp. (^{o}C)	Yield (%)	ref.
1.		1 mol % (S/C = 50)	8	Cs_2CO_3/ DMSO	80	93	[9c]
2.		1 mol % (S/C = 50)	4	Cs_2CO_3/ DMSO	80	81	[9a]
3.		0.2 mol % (S/C = 250)	16	K_3PO_4/ DMSO	90	>99	[9b]
4.	**2a–2b**	0.1 mol % (S/C = 1000)	10	K_3PO_4/ DMSO	90	96	**This work**
5.		0.15 mol % (S/C = 300)	48	Cs_2CO_3/ dioxane	130	>99	[15]
6.		10 mol % (S/C = 20)	24	Cs_2CO_3/ toluene	110	92	[6b]

Deprotonation of palladium coordinated phenylacetylene moiety **C** affords an intermediate **D**, which on further reductive elimination generates the palladium(II) species **A** and 2-(phenylethynyl)phenol. The product 2-(phenylethynyl)phenol becomes the substrate for the next catalytic cyclization step. On coordination with the palladium(II) species **A** giving the intermediate **E**, which undergoes oxidative addition followed by intermolecular rearrangement

produces intermediate **F**. Finally, the reductive elimination of the intermediate **F** gives the desired 2-phenylbenzofuran product along with the regeneration of initial palladium(II) species **A**.



Scheme 3. Possible mechanism for the tandem Heck alkynylation/cyclization reaction.

3. Conclusions

In summary, we have shown that the palladium pincer complex supported by 2,6-bis(pyrrolyl)pyridine ligand framework is an efficient catalytic system for one-pot tandem Heck alkynylation/cyclization reaction. The temperature effect on the one-pot tandem Heck alkynylation/cyclization reaction was studied. A variety of benzofuran derivatives were quantitatively synthesized using 0.1 mol % catalysts loading at 120 ^{o}C in 10 hours. These well-defined catalytic systems exhibit high performance in terms of product conversion, broad substrate scope, and high functional group tolerance. We believe that this catalytic process will expand the scope of pincer ligand assisted transition metal-catalyzed reaction in organic synthesis.

4. Experimental Sections:

4.1. General Methods and Materials.

All manipulations were carried out under an atmosphere of nitrogen or in air. NMR spectra were recorded at 298 K on Bruker 500 MHz and JEOL 400 MHz NMR spectrometer. The chemical shifts of proton and carbon are reported in ppm and referenced using residual proton (7.26 ppm) and carbon signals (77.16 ppm) of $CDCl_3$.[17] NMR annotations used: br. = broad, d = doublet, m = multiplet, s = singlet, t = triplet, sept = septet. Elemental analyses were performed using Thermo Quest FLASH 2000 SERIES (CHNS) Elemental Analyzer. Mass data are collected from Micromass Q-Tof spectrometer. All catalytic reactions were monitored on a Thermo Fisher Trace 1300 series GC system by GC-FID with a TG-IMS column of 30 m length, 0.25 mm diameter and 0.25 μm film thickness. Solvents were purchased from commercial suppliers and used without further purification. Catalytic substrates (2-iodophenol, 5-iodovanillin, 2-Iodo-3-hydroxypyridine, phenylacetylene, 4-ethynyltoluene, 3-ethynyltoluene, 4-ethylphenylacetylene, 4-*tert*-butylphenylacetylene, 4-ethynylanisole, 3-ethynylaniline), K_3PO_4 and $Pd(OAc)_2$ were purchased from Sigma-Aldrich and used as received without further purification. The ligands **1a**,[12] **1b**[13] and palladium complex **2b**[13] were prepared by reported literature procedures.

4.2. Synthesis of Pd-Pincer complex (2a)

A solution of ligand **1a** (0.115 g, 0.295 mmol) and $Pd(OAc)_2$ (0.066 g, 0.295 mmol) in CH_3CN (*ca*. 25 mL) was heated at 90 °C under nitrogen for 24 hours. After cooling to room temperature, the mixture was filtered through Celite and the filtrate was concentrated in a rotary evaporator. The collected pale yellow solid compound was washed further using hexane (2x5 mL) and dried under vacuum. The product **2a** was obtained as pale yellow solid (0.131 g, 82 % yield). ^{1}H NMR

(500 MHz, $CDCl_3$): δ 7.44-7.42 (m, 4H), 7.36 (br s, 4H), 7.26 (br s, 2H), 6.93 (t, 1H, J_{HH} = 7 Hz, py), 6.52 (s, 2H), 5.89 (s, 2H, pyrrolide-H), 2.44-2.30 (m, 6H, CH_3), 1.27 (s, 3H, CH_3CN) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 154.9, 141.0, 138.0, 137.3, 135.0, 129.7, 129.3, 128.1, 126.2, 111.3, 109.4, 16.12, 1.03. Anal. Calcd for $C_{29}H_{24}N_4Pd$: C, 65.11; H, 4.57; N, 10.47; Found: C, 64.68; H, 4.58; N, 9.44 %. HRMS (ESI) calcd. for $C_{29}H_{25}N_4Pd^+$ $[M+H]^+$ m/z 535.1114; Found 535.1114.

4.3. General Procedure for one-pot tandem Heck alkynylation/cyclization reaction

In a typical run, performed in air, a 25 mL of round bottom flask was charged with a mixture of 2-iodophenol (0.50 mmol), terminal alkyne (0.60 mmol), and K_3PO_4 (1.00 mmol). A palladium complex (**2a** or **2b**, 0.0005 mmol) was added to the mixture, followed by DMSO (*ca*. 2 mL) as a solvent, and then the reaction mixture was heated (either at 90 ^oC or at 120 ^oC) for 10 hours. The reaction mixture was cooled to room temperature, and water (*ca*. 20 mL) was added. The resulting mixture was extracted with EtOAc (*ca*. 50 mL). The organic layer was further extracted with EtOAc (*ca*. 2x20 mL). The organic layers were combined and vacuum dried to obtain a crude product that was subsequently purified by column chromatography. The obtained benzofuran derivatives (**3aa**–**3ap**) were characterized by NMR and Mass spectroscopy (See Supporting Information Figures S4-S23).

2-Phenylbenzo[b]furan (**3aa**: Table 2, entry 1): ^1H NMR (500 MHz, $CDCl_3$): δ 7.90-7.89 (m, 2H), 7.62-7.60 (m, 1H), 7.56-7.54 (m, 1H), 7.49-7.46 (m, 2H), 7.38 (t, 1H, J_{HH} = 7.0 Hz), 7.33-7.24 (m, 2H), 7.05 (s, 1H) ppm.[9b]

2-(p-tolyl)benzofuran (**3ab**: Table 2, entry 2): ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.84-7.82 (m, 2H), 7.64-7.58 (m, 2H), 7.34-7.30 (m, 4H), 7.03 (s, 1H), 2.46 (s, 3H) ppm.[9b]

2-m-Tolylbenzofuran (**3ac**: Table 2, entry 3): ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.74 (s, 1H), 7.71-7.70 (m, 1H), 7.62-7.60 (m, 1H), 7.57-7.55 (m, 1H), 7.38-7.36 (m, 1H), 7.35-7.29 (m, 1H), 7.28-7.25 (m, 1H), 7.24-7.19 (m, 1H), 7.03 (s, 1H), 2.46 (s, 3H) ppm.[9b]

2-(4-Ethylphenyl)benzofuran (**3ad**: Table 2, entry 4): ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.86 (d, 2H, J_{HH} = 8.0 Hz), 7.63 (d, 1H, J_{HH} = 8.0 Hz), 7.59 (d, 1H, J_{HH} = 8.0 Hz), 7.35-7.34 (m, 3H), 7.33-7.28 (m, 1H), 7.03 (s, 1H), 2.75-2.71 (m, 2H), 1.34 (t, 3H, J_{HH} = 8.0 Hz) ppm.[9b]

2-(4-tert-Butylphenyl)benzofuran (**3ae**: Table 2, entry 5): ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.81 (d, 2H, J_{HH} = 8.0 Hz), 7.58 (d, 1H, J_{HH} = 8.0 Hz), 7.53 (d, 1H, J_{HH} = 8.0 Hz), 7.48 (d, 2H, J_{HH} = 8.0 Hz), 7.29-7.22 (m, 2H), 6.99 (s, 1H), 1.37 (s, 9H) ppm.[9b]

2-(4-Methoxyphenyl)benzofuran (**3af**: Table 2, entry 6): ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.83 (d, 2H, J_{HH} = 8.0 Hz), 7.59 (d, 1H, J_{HH} = 7.0 Hz), 7.53 (d, 1H, J_{HH} = 8.0 Hz), 7.30-7.23 (m, 2H), 7.01 (d, 2H, J_{HH} = 8.0 Hz), 6.92 (s, 1H), 3.89 (s, 3H) ppm.[9b]

3-(benzofuran-2-yl)aniline (**3ag**: Table 2-3, entry 7 & 12): ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.60 (d, 1H, J_{HH} = 8.0 Hz), 7.55 (d, 1H, J_{HH} = 8.0 Hz), 7.32-7.27 (m, 2H), 7.26-7.23 (m, 3H), 7.00 (s, 1H), 6.70-6.69 (m, 1H), 3.68 (br s, 2H) ppm. ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 156.1, 154.8, 146.8, 131.4, 129.8, 129.3, 124.2, 122.9, 120.9, 115.5, 115.5, 111.3, 111.2, 101.3 ppm.[6e]

7-Methoxy-2-(phenyl)benzofuran-5-carbaldehyde (**3ah**: Table 2-3, entry 8 & 13): ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.99 (s, 1H), 7.87(d, 2H, J_{HH} = 7.5 Hz), 7.69 (s, 1H), 7.47-7.44 (m, 2H), 7.40-7.35 (m, 2H), 7.08 (s, 1H), 4.08 (s, 3H) ppm. $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 191.8, 157.8, 147.7, 146.1, 133.5, 130.8, 129.6, 129.2, 128.9, 125.2, 119.3, 104.6, 101.9, 56.2 ppm.[18]

7-Methoxy-2-(*p*-tolyl)benzofuran-5-carbaldehyde (**3ai**: Table 2-3, entry 9 & 14): ^{1}H NMR (500 MHz, $CDCl_3$): δ 10.00 (s, 1H), 7.79 (d, 2H, J_{HH} = 8.0 Hz), 7.71-7.70 (m, 1H), 7.36-7.35 (m, 1H), 7.28-7.26 (m, 2H), 7.04 (s, 1H), 4.09 (s, 3H), 2.41 (s, 3H) ppm. $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 191.9, 158.2, 147.6, 146.1, 139.5, 133.5, 131.1, 129.7, 126.9, 125.2, 119.3, 104.5, 101.2, 56.3, 21.5 ppm.[18]

7-methoxy-2-(4-methoxyphenyl)benzofuran-5-carbaldehyde (**3aj**: Table 2-3, entry 10 & 15): ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.93 (s, 1H), 7.76 (d, 2H, J_{HH} = 8.0 Hz), 7.61 (s, 1H), 7.28 (s, 1H), 6.92 (d, 2H, J_{HH} = 8.0 Hz), 6.88 (s, 1H), 4.03 (s, 3H), 3.81 (s, 3H) ppm. $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ 192.1, 160.7, 158.2, 147.7, 146.2, 133.7, 131.4, 127.0, 122.6, 119.2, 114.6, 104.6, 100.5, 56.5, 55.6 ppm.[19]

2-phenylfuro[2,3-*b*]pyridine (**3ak**: Table 2-3, entry 11 & 16): ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.52 (d, 1H, J_{HH} = 8.0 Hz), 7.92-7.90 (m, 2H), 7.77 (d, 1H, J_{HH} = 8.0 Hz), 7.50-7.47 (m, 2H), 7.43-7.40 (m, 1H), 7.23 (s, 1H), 7.22-7.19 (m, 1H) ppm. $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 159.7, 149.1, 148.1, 146.1, 129.8, 129.6, 129.0, 125.4, 118.9, 117.9, 102.5 ppm.[8a,20]

2-(4-Tolyl)-furo[3,2-*b*]pyridine (**3al**: Table 3, entry 17): ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.51-8.50 (m, 1H), 7.80 (d, 2H, J_{HH} = 8.0 Hz), 7.76-7.74 (m, 1H), 7.29 (d, 2H, J_{HH} = 8.0 Hz), 7.20-7.17 (m, 1H), 7.16 (s, 1H), 2.42 (s, 3H) ppm. $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ 160.0, 149.3, 148.0, 146.0, 139.9, 129.7, 127.1, 125.4, 118.6, 117.7, 101.8, 21.6 ppm.[21]

2-(4-ethylphenyl)furo[2,3-b]pyridine (**3am**: Table 3, entry 18): ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.52-8.50 (m, 1H), 7.83-7.82 (m, 2H), 7.76-7.74 (m, 1H), 7.30 (d, 2H, J_{HH} = 8.0 Hz), 7.20-7.18 (m, 1H), 7.17 (s, 1H), 2.71 (q, 2H, J_{HH} = 7.5 Hz), 1.28 (t, 3H, J_{HH} = 7.5 Hz) ppm. $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ 160.0, 149.2, 147.9, 146.2, 145.9, 128.5, 127.2, 125.4, 118.6, 117.7, 101.7, 31.0, 15.3 ppm. HRMS (ESI) calcd. for $C_{15}H_{14}NO^{+}$ $[M+H]^{+}$ *m*/z 224.1075; Found 224.1075.

2-(4-Methoxyphenyl)-furo[3,2-b]pyridine (**3an**: Table 3, entry 19): ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.49-8.48 (m, 1H), 7.84 (d, 2H, J_{HH} = 8.0 Hz), 7.73 (d, 1H, J_{HH} = 8.0 Hz), 7.18-7.15 (m, 1H), 7.08 (s, 1H), 7.01-6.99 (m, 2H), 3.87 (s, 3H) ppm. $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ 160.9, 159.9, 149.5, 147.9, 145.9, 127.0, 122.6, 118.3, 117.5, 114.5, 100.8, 55.5 ppm.[15,21]

3-(Furo[2,3-b]pyridin-2-yl)aniline (**3ao**: Table 3, entry 20): ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.54 (d, 1H, J_{HH} = 8.0 Hz), 7.77 (d, 1H, J_{HH} = 8.0 Hz), 7.33-7.30 (m, 1H), 7.29-7.7.28 (m, 1H), 7.25-7.21 (m, 1H), 7.20-7.19 (m, 2H), 6.77-6.75 (m, 1H), 3.35 (br.s, 2H) ppm. $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 207.2, 160.0, 149.1, 147.9, 147.0, 145.9, 130.6, 129.9, 117.8, 116.4, 115.8, 111.5, 102.3 ppm. HRMS (ESI) calcd. for $C_{13}H_{11}N_2O^{+}$ $[M+H]^{+}$ m/z 211.0871; Found 211.0871.

2-(4-Ethylphenyl)-7-methoxybenzofuran-5-carbaldehyde (**3ap**: Table 3, entry 21): ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.98 (s, 1H), 7.80 (d, 2H, J_{HH} = 7.0 Hz), 7.67(s, 1H), 7.34 (s, 1H), 7.29-7.28 (m, 2H), 7.01 (s, 1H), 4.08 (s, 3H), 2.70 (q, 2H, J_{HH} = 7.5 Hz), 1.27 (t, 3H, J_{HH} = 7.5 Hz) ppm. $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 191.8, 158.1, 147.6, 146.0, 145.7, 133.4, 131.0, 128.4, 127.0, 125.2, 119.2, 104.4, 101.2, 56.2, 28.8, 15.4 ppm. HRMS (ESI) calcd. for $C_{18}H_{17}O_3^+$ $[M+H]^+$ *m/z* 281.1177; Found 281.1176.

Conflicts of interest

There are no conflicts to declare

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Supplementary Data

Supplementary material related to this article can be found, in the online version, at DoI: https://doi.org/10.1016/j.tet.2020.XXXXXX.

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Highlights:

- Straightforward synthesis of [NNN] based palladium-pincer complexes as homogeneous catalysts in cross-coupling reactions.
- Excellent catalytic activity of bis(pyrrolyl)pyridine based palladium pincer complexes in one-pot tandem Heck alkynylation/cyclization reactions.
- The developed catalysts exhibit broad functional group compatibility and efficient conversion of benzofuran derivatives.