JOC The Journal of Organic Chemistry

Article

pubs.acs.org/joc

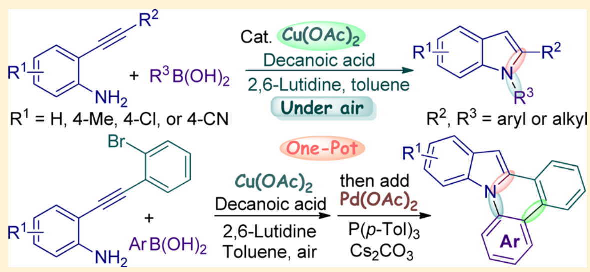
One-Pot Approach to 1,2-Disubstituted Indoles via Cu(II)-Catalyzed Coupling/Cyclization under Aerobic Conditions and Its Application for the Synthesis of Polycyclic Indoles

Jilong Gao, Yingying Shao, Jiaoyan Zhu, Jiaqi Zhu, Hui Mao, Xiaoxia Wang,* and Xin Lv*

Department of Chemistry, College of Chemistry and Life Sciences, Zhejiang Normal University, Jinhua 321004, People's Republic of China

Supporting Information

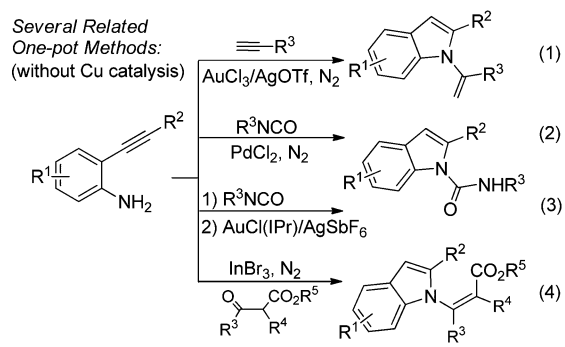
ABSTRACT: A straightforward assembly of 1,2-disubstituted indoles has been developed through a Cu(II)-catalyzed domino coupling/cyclization process. Under aerobic conditions, a wide range of 1,2-disubstituted indole derivatives were efficiently and facilely synthesized from 2-alkynylanilines and boronic acids. 2-(2-Bromoaryl)-1-aryl-1*H*-indoles, which were selectively generated in one pot under the Cu catalysis, afforded the indolo[1,2-*f*]phenanthridines via Pd-catalyzed intramolecular direct C(sp^2)−H arylation. The one-pot tandem approaches to the polycyclic indole derivatives were also successfully achieved.



INTRODUCTION

The indole nucleus is a key motif in numerous natural products, pharmaceutical agents, and functional materials.[1] The assembly of indole derivatives have attracted great interest.[2] Among the family of indoles, 1,2-disubstituted indoles are an important class of heterocycles because of their biological activities and medicinal applications.[3] Much attention has been focused on the synthesis of 1,2-disubstituted indole derivatives.[2b−e] A common route is the C−N bond-forming reaction of 2-substituted N−H indoles with an electrophile (e.g., alkyl/aryl halide).[4] However, 2-substituted N−H indoles should be prepared beforehand. Another popular method is the intramolecular annulation of *N*-substituted 2-alkynylanilines, while the amino group needs to be premodified.[5] The cyclization of *o*-*gem*-dihalovinylanilines also gives 1,2-disubstituted indoles.[6] Pd-catalyzed Larock heteroannulation is an important protocol for the assembly of indoles. This method generally results in 2,3-disubstituted ones.[7] Several domino or intramolecular approaches to 1,2-disubstituted indoles from 2-alkynylanilines have also been investigated.[8] For representative examples, Li et al. reported a Au(III)-catalyzed double-hydroamination reaction of *o*-alkynylanilines with terminal alkynes for the synthesis of *N*-alkenylindoles[8e] (Scheme 1, eq 1); Wu and co-workers described that $PdCl_2$-catalyzed tandem addition/cyclization reactions between 2-alkynylanilines and isocyanates furnished the corresponding *N*-carbamyl indole derivatives[8d] (eq 2); the Asensio group found that the *N*-carbamylindoles could also be prepared by the Au(I)-mediated intramolecular heterocyclization of 1-(*o*-ethynylaryl)ureas[8b] (eq 3); Fujioka et al. discovered an In(III)-promoted domino synthesis of *β*-(*N*-indolyl)-*α*,*β*-unsaturated esters from *o*-alkynylanilines and *β*-keto esters[8c] (eq 4). In spite of their efficiency, expensive, and/or air-sensitive promoters (such as Pd and Au catalysts) are usually employed.

Scheme 1. Several Previous Reports on the One-Pot Synthesis of 1,2-Disubstituted Indoles from 2-Alkynylanilines

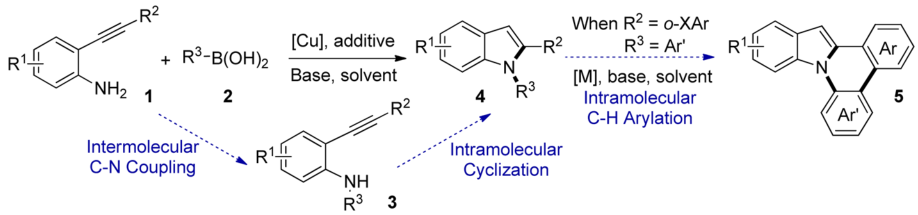


And notably, most of these protocols require the protection of inert gas and rigid manipulations. The development of facile, versatile, and practical approaches to 1,2-disubstituted indoles just under aerobic conditions still remains as a challenge.

On the other hand, indolo[1,2-*f*]phenanthridines, which incorporate indole and phenanthridine skeletons, are useful polycyclic indole derivatives and may be utilized for organic light-emitting diodes (OLEDs)[9] and dye-sensitized solar cells (DSSCs).[10] However, although these polycyclic heterocycles have promising applications, efficient and facile synthetic routes are rarely documented until now.[10−12] One-pot approaches to these polycyclic heterocycles have been developed. It was reported that Pd-catalyzed cascade reactions of arynes with

Received: June 4, 2014
Published: September 11, 2014

Scheme 2. Proposed One-Pot Approach to 1,2-Disubstituted Indoles and Indolo[1,2-*f*]phenanthridines



N-(*o*-bromophenyl)indoles afforded the corresponding indolo-[1,2-*f*]phenanthridines.[10,11] These polyheterocycles can also be assembled via Pd-catalyzed tandem C−H/N−H coupling between 2-arylindoles and *o*-dihaloarenes.[12] Compared with the traditional stepwise routes, the methods provide more convenient and efficient approaches to these heterocycles. However, both protocols employed special materials, such as arynes, *N*-(*o*-bromophenyl)indoles, and 2-arylindoles; thus, the application scope may be limited to a certain degree.

Because of the convenience, low cost, and high efficiency, Cu-mediated domino reactions have been known as powerful tools for direct assembly of structurally diversified molecules in one pot.[13] The domino *N*-arylation/hydroamination of *o*-alkynylhaloarenes with primary amines generated 1,2-disubstituted indoles directly, while complex preligands and strong bases were usually utilized.[14] Recently, Miura and coworkers found that *o*-alkynlanilines and azoles underwent a Cu-catalyzed C−H arylation/annulation to afford the *N*-azolylindoles (under O_2 atmosphere).[15] Tang et al. prepared *N*-indolyl- or *N*-benzofuranylindoles through Cu-mediated tandem reactions between 2-alkynylcyclohexadienimines/cyclohexadienones and *o*-alkynylanilines.[16] Both pathways directly gave the *N*-heteroarylindoles.

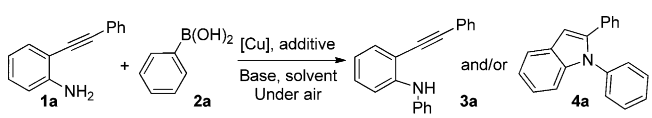
Cu-mediated amination of boronic acids (Chan−Lam coupling) is an attractive C−N bond-forming protocol, partially because boronic reagents are easily accessible, low toxic, and air and moisture stable.[17] To the best of our knowledge, there is no report on the Cu-mediated domino generation of 1,2-disubstituted indoles from *o*-alkynylanilines and boronic acids. As part of our continuing efforts in synthesizing *N*-heterocycles through Cu-mediated one-pot reactions,[18] we report a domino approach to 1,2-disubstituted indoles under aerobic conditions based on a Cu-catalyzed domino Chan−Lam coupling/cyclization process and its application for the tandem assembly of indolo[1,2-*f*]phenanthridines.

We envisaged that the scaffold of 1,2-disubstituted indoles could be readily constructed through a copper-mediated domino reaction between 2-alkynylanilines **1** and boronic acids **2** (Scheme 2). The domino process may be initiated by a Cu-catalyzed intermolecular C−N bond formation to generate intermediate **3**, and the subsequent intramolecular heteroannulation under the same Cu catalysis affords the corresponding 1,2-disubstituted indole **4** in one pot. Furthermore, the intramolecular C−H arylation of the *o*-haloaryl-containing products would give the polycyclic indolo[1,2-*f*]phenanthridine **5** under the proper conditions.

■ RESULTS AND DISCUSSION

On the basis of the above hypothesis, we commenced our investigation with the model reaction between 2-(phenylethynyl)-aniline **1a** and phenylboronic acid **2a**. Initially, the reaction was performed in the presence of $Cu(OAc)_2$ (10 mol %), 1,10-phenanthroline (1,10-phen, 20 mol %), and K_2CO_3 (1.5 equiv) in refluxing toluene under air atmosphere. However, neither intermediate **3a** nor the desired product **4a** was generated (Table 1, entry 1). Switching the additive to DMG and the base to pyridine did not improve the result (entry 2). To our delight, a moderate yield of the desired cyclized product was obtained when decanoic acid was used as the additive (entry 3).[19] DMAP and Cs_2CO_3 were inferior to pyridine (entries 4 and 5). 2,6-Lutidine acted as the most efficient and afforded **4a** in a good yield (entry 6). Further study indicated that the heating process also significantly affected the results. Only intermediate **3a** (70% yield) could be isolated when the mixture was just stirred at room temperature (entry 7). Increasing the temperature to 60 °C after prestir did not give obvious improvement (entry 8). However, when the

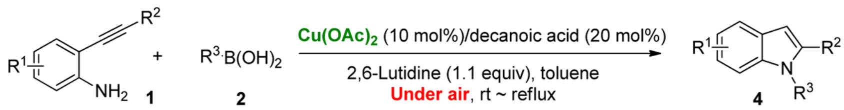
Table 1. Optimization of the Reaction Conditions[a]



entry	catalyst	additive	base	solvent	yield of 4a[b] (%)
1	$Cu(OAc)_2$	1,10-phen	K_2CO_3	toluene	nd[c]
2	$Cu(OAc)_2$	DMG[d]	pyridine	toluene	nd
3	$Cu(OAc)_2$	decanoic acid	pyridine	toluene	53
4	$Cu(OAc)_2$	decanoic acid	DMAP	toluene	45
5	$Cu(OAc)_2$	decanoic acid	Cs_2CO_3	toluene	trace
6	$Cu(OAc)_2$	decanoic acid	2,6-lutidine	toluene	78
7	$Cu(OAc)_2$	decanoic acid	2,6-lutidine	toluene	*e*
8	$Cu(OAc)_2$	decanoic acid	2,6-lutidine	toluene	trace[f]
9	$Cu(OAc)_2$	decanoic acid	2,6-lutidine	toluene	88[g]
10	$Cu(OAc)_2$	myristic acid	2,6-lutidine	toluene	85[g]
11	CuI	decanoic acid	2,6-lutidine	toluene	42[g]
12	$Cu(OTf)_2$	decanoic acid	2,6-lutidine	toluene	81[g]
13	$CuBr_2$	decanoic acid	2,6-lutidine	toluene	63[g]
14	$CuCl_2$	decanoic acid	2,6-lutidine	toluene	72[g]
15	$Cu(OAc)_2$	decanoic acid	2,6-lutidine	*o*-xylene	78[g]
16	$Cu(OAc)_2$	decanoic acid	2,6-lutidine	EGME[h]	trace[g]
17	$Cu(OAc)_2$	decanoic acid	2,6-lutidine	dioxane	48[g]
18	$Cu(OAc)_2$	decanoic acid	2,6-lutidine	DMF	40[g]
19	$Cu(OTf)_2$	decanoic acid	2,6-lutidine	DCE	67[g]
20	$Cu(OAc)_2$	decanoic acid	2,6-lutidine	toluene	88[g,i]
21	$Cu(OAc)_2$	decanoic acid	2,6-lutidine	toluene	58[g,i,j]

[a]Reaction conditions: 2-(phenylethynyl)aniline (1.0 mmol), phenylboronic acid (1.5 mmol), Cu catalyst (0.1 mmol, 10 mol %), additive (0.2 mmol, 20 mol %), base (1.5 mmol, 1.5 equiv), in solvent (3 mL), under air, at reflux for 24 h. [b]Isolated yield (when intermediate **3a** was consumed almost completely) or yield based on ^{1}H NMR (when **3a** remained). Since the polarities of **3a** and **4a** were very close to each other, their mixture could not be well separated by chromatography. [c]nd = not detected. [d]DMG = *N*,*N*-dimethylglycine. [e]At rt for 24 h. Only intermediate **3a** (70% yield) was obtained. [f]At rt for 8 h, then at 60 °C for 16 h. [g]At rt for 8 h, then at reflux for 16 h. [h]EGME = ethylene glycol monoethyl ether. [i]1.1 equiv of 2,6-lutidine was utilized. [j]Under N_2 atmosphere.

Table 2. Copper(II)-Catalyzed One-Pot Synthesis of 1,2-Disubstituted Indoles[a]



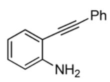
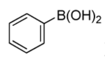
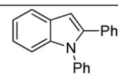
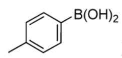
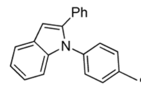
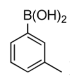
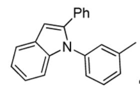
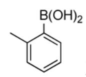
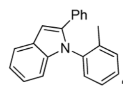
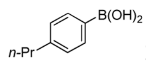
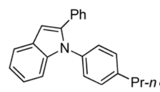
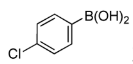
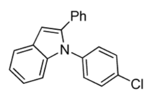
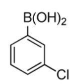
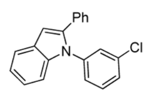
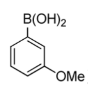
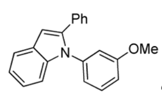
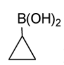
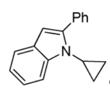
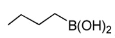
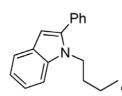
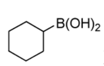
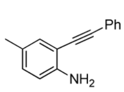
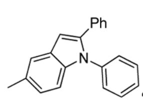
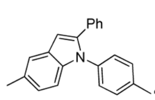
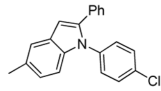
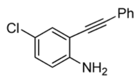
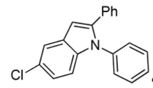
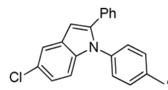
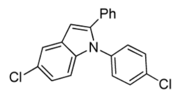
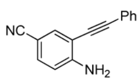
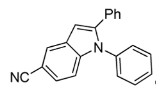
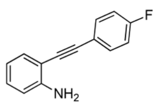
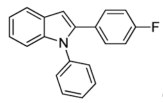
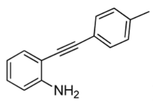
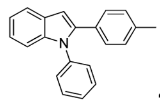
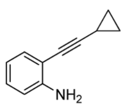
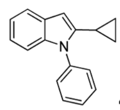
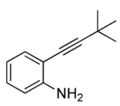
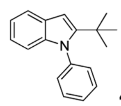
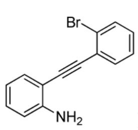
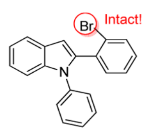
Entry	Substrate **1**	Boronic acid **2**	Product **4**	Time (h)	Yield (%)[b]
1	 **1a**	 **2a**	 **4a**	24	88
2	**1a**	 **2b**	 **4b**	24	91
3	**1a**	 **2c**	 **4c**	24	90
4	**1a**	 **2d**	 **4d**	28	57
5	**1a**	 **2e**	 **4e**	28	82
6	**1a**	 **2f**	 **4f**	24	69
7	**1a**	 **2g**	 **4g**	24	54
8	**1a**	 **2h**	 **4h**	24	73
9	**1a**	 **2i**	 **4i**	40	55
10	**1a**	 **2j**	 **4j**	42	43[c]
11	**1a**	 **2k**	-	48	trace
12	 **1b**	**2a**	 **4k**	26	85
13	**1b**	**2b**	 **4l**	30	90

Table 2. continued

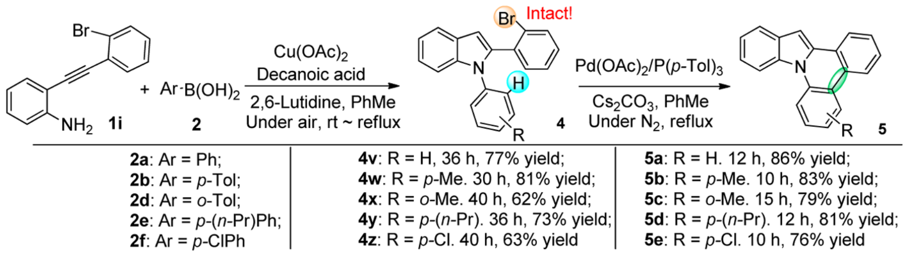
Entry	Substrate **1**	Boronic acid **2**	Product **4**	Time (h)	Yield (%)[b]
14	**1b**	**2f**	 **4m**	30	72
15	 **1c**	**2a**	 **4n**	30	66
16	**1c**	**2b**	 **4o**	30	78
17	**1c**	**2f**	 **4p**	36	53
18	 **1d**	**2a**	 **4q**	30	48
19	 **1e**	**2a**	 **4r**	24	70
20	 **1f**	**2a**	 **4s**	24	85
21	 **1g**	**2a**	 **4t**	24	64
22	 **1h**	**2a**	 **4u**	24	61
23	 **1i**	**2a**	 **4v**	36	77

[a]Reaction conditions: 2-alkynylaniline (1.0 mmol), boronic acid (1.5 mmol), $Cu(OAc)_2$ (0.1 mmol, 10 mol %), decanoic acid (0.2 mmol, 20 mol %), 2,6-lutidine (1.1 mmol, 1.1 equiv), in toluene (3 mL), under air, at rt for about 8 h, then at reflux for 16−40 h. [b]Isolated yield (%). [c]Myristic acid was used as the additive instead of decanoic acid.

mixture was heated at reflux (120 °C) after being prestirred at room temperature, an excellent yield of the desired substituted indole was obtained (entry 9). Another additive, myristic acid,[20] was slightly inferior to decanoic acid (entry 10). We investigated other copper sources including CuI, $Cu(OTf)_2$, $CuBr_2$,and $CuCl_2$ and identified $Cu(OAc)_2$ as the most efficient catalyst (compare entry 9 with entries 11−14). Different solvents were also screened, and toluene proved to be the optimal solvent (compare entry 9 with entries 15−19). Further investigation found that 1.1 equiv of the base was adequate for this domino transformation (entry 20). A control experiment under nitrogen conditions showed that the reaction was much more efficient under air atmosphere (entry 21), indicating that oxygen might play an important role in the transformation.

After the optimized conditions had been established, the scope of the Cu-mediated domino synthesis was investigated by using a variety of 2-alkynylanilines and boronic acids (Table 2). A range of arylboronic acids were utilized. Generally, both electron-donating groups (*p*-Me, *m*-Me, *o*-Me, *p*-Pr, and *m*-OMe) and electron-withdrawing groups (*p*-Cl and *m*-Cl) on the phenyl rings of the reagents could be well tolerated, and moderate to excellent yields of the desired *N*-arylindoles were obtained (entries 1−8). The Suzuki reagent bearing an *ortho*-substituent or an electron-withdrawing substituent showed relatively lower reactivity (entries 4, 6, and 7). We also investigated several alkylboronic acids and found that they were inferior to arylboronic reagents (entries 9−11). Cyclopropylboronic acid **2i** reacted with **1a** to afford a moderate yield (entry 9);

Scheme 3. Cu-Mediated Domino Synthesis of *o*-Brominated Indoles and Their Derivation to Indolo[1,2-*f*]phenanthridines via Pd-Catalyzed Intramolecular C−H Arylation

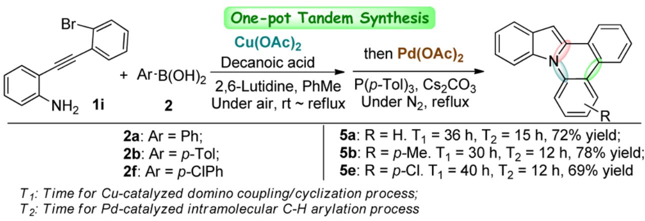


the reaction with primary alkylboronic acid **2j** gave a lower yield (entry 10); but the use of secondary alkylboronic acid **2k** resulted in only a trace amount of the product (entry 11). Notably, among the alkylboronic acids tested, **2i** acted as the most active reagent, probably because of its special character associated with the ring strain. Various groups on the 2-alkynylanilines were also examined (entries 12, 15, and 18−23). Either electron-donating group (Me) or electron-withdrawing group (Cl) on the aryl ring of the aniline is compatible with the reaction conditions (entries 12−17). However, the strong electron-withdrawing substituent (CN) has a negative effect (entry 18). Different substituents on the ethynyl chain of the 2-alkynylanilines were also studied, and it was found that both the substrates with aryl groups (including Ph, *p*-Tol, *p*-FPh, and *o*-BrPh) and those bearing alkyl groups (including cyclopropyl and *t*-Bu) on the ethynyl allowed the reaction to proceed smoothly to furnish the desired 1,2-disubstituted indoles (entries 1 and 19−23).

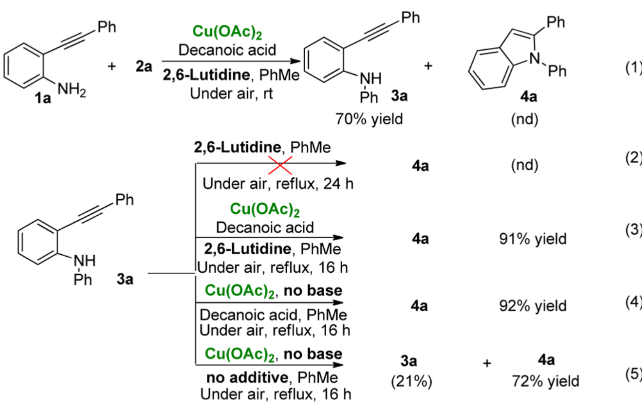
It is noticeable that the *ortho*-bromide is also compatible under these conditions, and the remaining *o*-C−Br bond would provide an additional opportunity for the further derivation (Table 2, entry 23). Considering that the intramolecular direct sp^2 C−H arylation of the *o*-brominated 1,2-diaryl indoles may lead to the assembly of the corresponding indolo[1,2-*f*]-phenanthridine, which might be useful in the field of material,[9,10] we then tend to transform compound **4v** into the polycyclic indole derivative **5a**. Fortunately, the proposed intramolecular cyclization was successfully achieved under proper Pd catalysis ($Pd(OAc)_2/P(p\text{-Tol})_3/Cs_2CO_3$/PhMe). Encouraged by these results, we next turned to synthesize several substituted indoles with an *o*-BrPh group by using the above Cu(II)-catalyzed domino protocol (see Scheme 3, the synthesis of **4w−z**) and applied them to the assembly of the polyheterocycles, respectively. These indoles also smoothly underwent the Pd-mediated intramolecular C−H arylation, and desired indolo[1,2-*f*]phenanthridines **5** were delivered in good yields (see Scheme 3, the assembly of **5b−e**).

In order to further facilitate the procedures of the method and make it more practical, we attempted to perform the above two-step reactions in one pot. Our investigation showed that the tandem synthesis of the indolo[1,2-*f*]phenanthridines was feasible. During the preliminary studies, the reaction of **1i** with **2a** was chosen as the model reaction to examine the conditions. When the formation of **4v** was complete, $Pd(OAc)_2$, $P(p\text{-Tol})_3$, and Cs_2CO_3 were added to the reaction mixture (under N_2) without isolation of **4v**, and indolo[1,2-*f*]phenanthridine **5a** was successfully generated in a good yield (for details, see the Experimental Section). Under the modified conditions, different arylboronic acids were used to study the scope of this one-pot synthesis (Scheme 4). All three boronic acids tested successfully reacted with **1i**, affording the desired indolo-[1,2-*f*]phenanthridines in moderate to good yields.

Scheme 4. One-Pot Tandem Synthesis of Indolo[1,2-*f*]phenanthridines



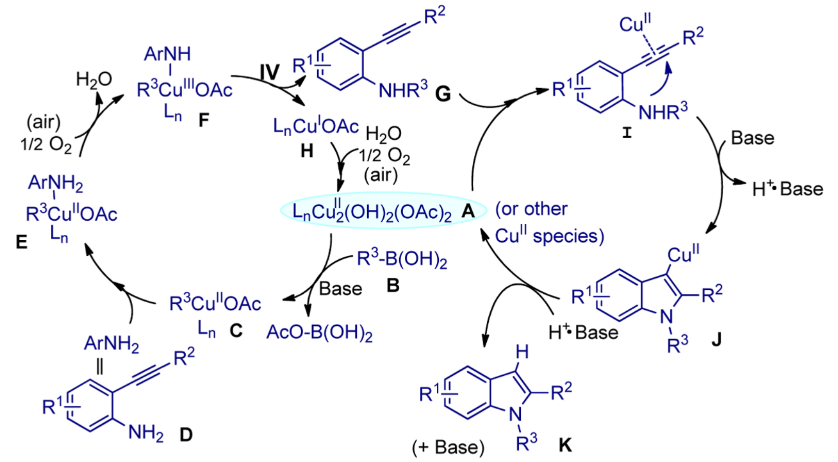
Scheme 5. Several Control Experiments



To gain insight into the mechanism of the coupling/cyclization process, several additional control experiments were also performed (Scheme 5). Under the promotion of $Cu(OAc)_2$/decanoic acid/2,6-lutidine, the reaction of **1a** with **2a** at room temperature only delivered intermediate **3a** in 70% yield, and no desired product **4a** was observed (Scheme 5, eq 1). The transformation of the isolated intermediate was then subjected to different conditions (eq 2−4). Without the addition of Cu(II) catalyst, no desired indole was generated and only the intermediate was recovered (eq 2), indicating that the Cu(II) catalyst was indispensable for this intramolecular cyclization process. However, in the presence of $Cu(OAc)_2$, the heterocyclization was efficiently achieved, with or without the addition of 2,6-lutidine (eq 3 and 4), showing that external base was unnecessary for the Cu(II)-mediated intramolecular annulation. Further investigation implied that the addition of decanoic acid also facilitated the cyclization process to a certain degree (eq 5 vs eq 4), probably due to the enhancement of the solubility of the Cu(II) catalyst by coordination.[17c]

On the basis of our observations and the relevant reports,[5h,i,17a,c] a possible mechanism for the coupling/annulation under aerobic conditions was proposed in Scheme 6. Under the promotion of base (such as 2,6-lutidine), Cu(II) complex **A**[17a]

Scheme 6. Possible Mechanism for Cu(II)-Catalyzed Coupling/Cyclization Reaction



would transmetalate with boronic acid **B** to afford R−Cu(II) species **C**. Complex **C** coordinated with aniline **D** to give Cu(II) complex **E**, which was then converted into Cu(III) complex **F** through oxidation by dioxygen (from air). Complex **F** underwent a reductive elimination to furnish coupling product **G** and Cu(I) complex **H**. And the oxidation of **H** regenerated Cu(II) species **A**. Then the Cu(II) complex might coordinate with the C−C triple bond of coupling product **G** to form Cu(II) complex **I**,[5h,i] and the alkyne was electrophilically activated. Finally, the intramolecular cyclization followed by protonolysis would provide the corresponding 1,2-disubstituted indole **K** along with the regenerated Cu(II) species.

■ CONCLUSIONS

In conclusion, we have developed a novel single-step approach to 1,2-disubstituted indoles through Cu(II)-catalyzed domino-coupling/cyclization reactions of 2-alkynylanilines and boronic acids. Under inexpensive Cu catalysis and aerobic conditions, a wide range of the desired 1,2-disubstituted indoles were conveniently and efficiently synthesized, and the *o*-Br-containing indoles were also selectively assembled in one pot. The potential of this indole synthesis is presented by its aerobic conditions, wide application scope, and simple manipulation. Moreover, the *o*-brominated products could be transformed into indolo[1,2-*f*]-phenanthridines via Pd-catalyzed intramolecular direct C(sp^2)−H arylation. One-pot tandem synthesis of the polycyclic indole derivatives was also successfully achieved under sequential Cu/Pd catalysis. The method may be a useful and practical tool for the assembly of relevant *N*-heterocyclic molecules of interest in medicinal chemistry and material science.

■ EXPERIMENTAL SECTION

General Information. Unless otherwise noted, all one-pot reactions were carried out in an overdried Schlenk tube equipped with a magnetic stir bar under aerobic atmosphere. Toluene, *o*-xylene, and dioxane were distilled from Na; DMF and DCE were distilled from CaH_2. 2-Alkynylanilines **1** were synthesized according to the known literature.[21] All other reagents were received from commercial sources and utilized without further purification, if not stated otherwise. All melting points are uncorrected. The NMR spectra were recorded in $CDCl_3$ on a 400 MHz or 600 MHz instrument with TMS as internal standard. Chemical shifts (δ) were reported in parts per million (ppm) downfield from TMS. Data are represented as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, b = broad), coupling constant (*J*, Hz), and integration. Thin-layer chromatography (TLC) was performed with 0.2 mm thick silica gel plates (GF254). Visualization was accomplished by UV light. The columns were hand packed with silica gel 60 (160−200 mesh). Unknown products were additionally confirmed by high-resolution mass spectra (HRMS) using a TOF-MS instrument with an ESI source.

General Procedure for Cu-Catalyzed One-Pot Synthesis of 1,2-Disubstituted Indoles 4. An oven-dried Schlenk tube was charged with a magnetic stir bar, 2-alkynylaniline **1** (1.0 mmol, 1 equiv), boronic acid **2** (1.5 mmol, 1.5 equiv), $Cu(OAc)_2$ (0.1 mmol, 10 mol %), and decanoic acid (0.2 mmol, 20 mol %). A solution of 2,6-lutidine (1.1 mmol, 1.1 equiv) in toluene (3 mL) was added via syringe. The tube was sealed and allowed to stir at room temperature for about 8 h (monitored by TLC). Then the mixture was stirred at 120 °C for 16−40 h. After being cooled to room temperature, the mixture was diluted with ethyl acetate (30 mL), filtered through a plug of silica gel, and concentrated. The residue was purified by column chromatography on silica gel using petroleum ether/EtOAc (50:1 → 20:1, v:v) as eluent to give product **4**.

1,2-Diphenyl-1H-indole (4a):[6b] white solid (237 mg, 88% yield); mp 78−79 °C (lit.[6b] mp 78−80 °C); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.65−7.68 (m, 1H), 7.35−7.37 (m, 2H), 7.27−7.30 (m, 2H), 7.24−7.26 (m, 2H) 7.18−7.23 (m, 5H), 7.15−7.16 (m, 2H), 6.79 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 140.8, 139.1, 138.6, 132.7, 129.4 (2C), 129.0 (2C), 128.4, 128.3 (2C), 128.2 (2C), 127.4, 127.3, 122.5, 120.8, 120.7, 110.7, 103.8.

2-Phenyl-1-(p-tolyl)-1H-indole (4b):[22] pale yellow solid (258 mg, 91% yield); mp 80−82 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.67−7.69 (m, 1H), 7.27−7.28 (m, 3H), 7.23−7.25 (m, 3H), 7.19−7.21 (m, 2H), 7.16−7.17 (m, 2H), 7.12−7.13 (m, 2H), 6.79 (s, 1H), 2.39 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 140.9, 139.2, 137.1, 136.0, 132.7, 130.0 (2C), 129.0 (2C), 128.3, 128.26 (2C), 127.9 (2C), 127.4, 122.3, 120.7, 120.6, 110.8, 103.5, 21.3.

2-Phenyl-1-(m-tolyl)-1H-indole (4c):[22] white solid (255 mg, 90% yield); mp 91−93 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65−7.67 (m, 1H), 7.24−7.27 (m, 3H), 7.17−7.22 (m, 4H), 7.13−7.16 (m, 2H), 7.07−7.11 (m, 2H), 6.97−6.99 (m, 1H), 6.78 (s, 1H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.8, 139.3, 139.2, 138.5, 132.7, 129.1, 128.9 (2C), 128.6, 128.3, 128.2 (2C), 128.1, 127.3, 125.3, 122.3, 120.7, 120.6, 110.8, 103.7, 21.5.

2-Phenyl-1-(o-tolyl)-1H-indole (4d): yellow oil (162 mg, 57% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68−7.70 (m, 1H), 7.30−7.34 (m, 1H), 7.26−7.28 (m, 5H), 7.20−7.23 (m, 3H), 7.12−7.17 (m, 2H), 6.93−6.95 (m, 1H), 6.83 (s, 1H), 1.86 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.2, 139.1, 137.7, 137.0, 132.8, 131.3, 129.6, 128.5, 128.34 (2C), 128.31 (2C), 128.26, 127.4, 127.0, 122.3, 120.5 (2C), 110.9, 102.7, 17.7; HRMS (ESI) calcd for $C_{21}H_{18}N$ (M + H$^+$) 284.1434, found 284.1439.

2-Phenyl-1-(4-propylphenyl)-1H-indole (4e): pale yellow solid (255 mg, 82% yield); mp 83−84 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.66−7.68 (m, 1H), 7.26−7.29 (m, 3H), 7.19−7.24 (m, 5H), 7.14−7.17 (m, 4H), 6.79 (s, 1H), 2.60−2.63 (m, 2H), 1.64−1.69 (m, 2H), 0.93–0.97 (m, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 141.9, 140.9, 139.2, 136.1, 132.7, 129.4 (2C), 129.0 (2C), 128.3, 128.2 (2C), 127.9 (2C), 127.3, 122.3, 120.7, 120.6, 110.8, 103.5, 37.7, 24.5, 13.9; HRMS (ESI) calcd for $C_{23}H_{22}N$ (M + H$^+$) 312.1747, found 312.1742.

1-(4-Chlorophenyl)-2-phenyl-1H-indole (**4f**):[23] yellow solid (210 mg, 69% yield); mp 100–102 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.69–7.70 (m, 1H), 7.36–7.38 (m, 2H), 7.22–7.29 (m, 6H), 7.17–7.20 (m, 4H), 6.79–6.82 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 140.7, 138.9, 137.2, 132.9, 132.5, 132.3, 129.6 (2C), 129.3 (2C), 129.0 (2C), 128.4 (2C), 127.6, 122.7, 121.1, 120.8, 110.5, 104.3.

1-(3-Chlorophenyl)-2-phenyl-1H-indole (**4g**): yellow solid (164 mg, 54% yield); mp 115–117 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.67–7.70 (m, 1H), 7.29–7.33 (m, 4H), 7.25–7.27 (m, 5H), 7.18–7.22 (m, 2H), 7.07–7.09 (m, 1H), 6.80 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 140.7, 139.9, 138.9, 134.9, 132.2, 130.4, 129.0 (2C), 128.48, 128.46 (2C), 128.1, 127.7, 127.6, 126.5, 122.8, 121.2, 120.8, 110.5, 104.4; HRMS (ESI) calcd for $C_{20}H_{15}ClN$ (M + H$^+$) 304.0888, found 304.0895.

1-(3-Methoxyphenyl)-2-phenyl-1H-indole (**4h**): white solid (219 mg, 73% yield); mp 95–97 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.68–7.69 (m, 1H), 7.35–7.37 (m, 1H), 7.27–7.31 (m, 3H), 7.21–7.26 (m, 3H), 7.17–7.19 (m, 2H), 6.86–6.88 (m, 1H), 6.80–6.84 (m, 3H), 3.68 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 160.2, 140.8, 139.6, 139.0, 132.6, 130.0, 128.9 (2C), 128.34, 128.28 (2C), 127.4, 122.5, 120.8, 120.7, 120.4, 113.6, 113.2, 110.8, 103.8, 55.4; HRMS (ESI) calcd for $C_{21}H_{18}NO$ (M + H$^+$) 300.1383, found 300.1392.

1-Cyclopropyl-2-phenyl-1H-indole (**4i**): yellow oil (128 mg, 55% yield); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.60–7.64 (m, 4H), 7.44 (t, J = 7.6 Hz, 2H), 7.37–7.38 (m, 1H), 7.22–7.24 (m, 1H), 7.13 (t, J = 7.6 Hz, 1H), 6.53 (s, 1H). 3.45–3.48 (m, 1H), 0.95–0.99 (m, 2H), 0.66–0.69 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 141.9, 133.6, 129.5, 128.9 (2C), 128.3 (2C), 127.8, 127.6, 121.7, 120.6, 120.1, 111.1, 102.0, 26.2, 9.2 (2C); HRMS (ESI) calcd for $C_{17}H_{16}N$ (M + H$^+$) 234.1277, found 234.1285.

1-Butyl-2-phenyl-1H-indole (**4j**):[24] yellow solid (107 mg, 43% yield); mp 104–106 °C (lit.[24] mp 105–106 °C); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.63 (d, J = 7.6 Hz, 1H), 7.47–7.48 (m, 2H), 7.42–7.45 (m, 2H), 7.37–7.39 (m, 2H), 7.20–7.23 (m, 1H), 7.11–7.13 (m, 1H), 6.51 (s, 1H), 4.13 (t, J = 7.5 Hz, 2H), 1.63–1.68 (m, 2H), 1.13–1.19 (m, 2H), 0.78 (t, J = 7.4 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 141.5, 137.5, 133.4, 129.6 (2C), 128.6 (2C), 128.3, 128.0, 121.6, 120.7, 119.8, 110.2, 102.2, 43.8, 32.2, 20.1, 13.7.

5-Methyl-1,2-diphenyl-1H-indole (**4k**):[24] pale yellow solid (241 mg, 85% yield); mp 88–90 °C (lit.[24] mp 89–92 °C); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.47 (s, 1H), 7.38–7.41 (m, 2H), 7.31–7.34 (m, 1H), 7.19–7.27 (m, 8H), 7.00–7.01 (m, 1H), 6.73 (s, 1H), 2.47 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 140.8, 138.8, 137.6, 132.8, 130.1, 129.3 (2C), 129.0 (2C), 128.6, 128.3 (2C), 128.1 (2C), 127.3, 127.2, 124.0, 120.3, 110.4, 103.4, 21.5.

5-Methyl-2-phenyl-1-(p-tolyl)-1H-indole (**4l**): yellow solid (268 mg, 90% yield); mp 127–129 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.45 (s, 1H), 7.25–7.27 (m, 2H), 7.19–7.23 (m, 3H), 7.14–7.18 (m, 3H), 7.10–7.11 (m, 2H), 6.97–6.99 (m, 1H), 6.70 (s, 1H), 2.45 (s, 3H), 2.37 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 140.9, 137.7, 137.0, 136.2, 132.9, 130.0 (2C), 129.0 (2C), 128.9, 128.5, 128.2 (2C), 127.8 (2C), 127.2, 123.9, 120.2, 110.5, 103.1, 21.5, 21.3; HRMS (ESI) calcd for $C_{22}H_{20}N$ (M + H$^+$) 298.1590, found 298.1598.

1-(4-Chlorophenyl)-5-methyl-2-phenyl-1H-indole (**4m**): yellow solid (229 mg, 72% yield); mp 138–140 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.46 (s, 1H), 7.36–7.38 (m, 2H), 7.24–7.26 (m, 5H), 7.15–7.17 (m, 3H), 7.01–7.02 (m, 1H), 6.72 (s, 1H), 2.47 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 140.7, 137.4, 132.8, 132.5, 130.4, 129.6 (2C), 129.5, 129.2 (2C), 129.0 (2C), 128.7, 128.4 (2C), 127.5, 124.3, 120.4, 110.2, 103.9, 21.5; HRMS (ESI) calcd for $C_{21}H_{17}ClN$ (M + H$^+$) 318.1044, found 318.1059.

5-Chloro-1,2-diphenyl-1H-indole (**4n**): yellow solid (200 mg, 66% yield); mp 136–137 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.62–7.63 (m, 1H), 7.38–7.41 (m, 2H), 7.34 (t, J = 7.4 Hz, 1H), 7.20–7.23 (m, 7H), 7.16–7.18 (m, 1H), 7.09–7.11 (m, 1H), 6.72 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 142.1, 138.2, 137.5, 132.1, 129.5 (2C), 129.3, 129.0 (2C), 128.4 (2C), 128.0 (2C), 127.8, 127.6, 126.3, 122.6, 119.9, 111.8, 103.1; HRMS (ESI) calcd for $C_{20}H_{15}ClN$ (M + H$^+$) 304.0888, found 304.0897.

5-Chloro-2-phenyl-1-(p-tolyl)-1H-indole (**4o**): yellow solid (248 mg, 78% yield); mp 111–113 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.61 (m, 1H), 7.21–7.23 (m, 5H), 7.17–7.18 (m, 2H), 7.14–7.15 (m, 1H), 7.06–7.08 (m, 3H), 6.69 (s, 1H), 2.37 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 142.1, 137.5, 135.5, 132.2, 130.1 (2C), 129.2, 129.0 (2C), 128.3 (2C), 127.74 (2C), 127.67, 126.2, 122.5, 121.7, 119.8, 111.8, 102.9, 21.3; HRMS (ESI) calcd for $C_{21}H_{17}ClN$ (M + H$^+$) 318.1044, found 318.1047.

5-Chloro-1-(4-chlorophenyl)-2-phenyl-1H-indole (**4p**): yellow solid (179 mg, 53% yield); mp 134–135 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.63–7.64 (m, 1H), 7.38–7.39 (m, 2H), 7.27–7.28 (m, 3H), 7.22–7.24 (m, 2H), 7.15–7.16 (m, 3H), 7.12–7.14 (m, 1H), 6.72 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 142.0, 136.8, 133.4, 132.5, 131.8, 129.8 (2C), 129.2 (2C), 129.1 (2C), 128.5 (2C), 128.0, 126.6, 122.9, 121.7, 120.1, 111.5, 103.6; HRMS (ESI) calcd for $C_{20}H_{14}Cl_2N$ (M + H$^+$) 338.0498, found 338.0508.

1,2-Diphenyl-1H-indole-5-carbonitrile (**4q**): yellow solid (141 mg, 48% yield); mp 158–160 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.02 (s, 1H), 7.43–7.46 (m, 2H), 7.38–7.42 (m, 3H), 7.29–7.30 (m, 1H), 7.23–7.27 (m, 6H), 6.84 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 143.3, 140.5, 137.5, 131.5, 130.0, 129.7 (2C), 129.1 (2C), 128.5 (2C), 128.23, 128.22, 128.1, 128.0 (2C), 126.1, 125.3, 120.8, 111.6, 103.8; HRMS (ESI) calcd for $C_{21}H_{15}N_2$ (M + H$^+$) 295.1230, found 295.1237.

2-(4-Fluorophenyl)-1-phenyl-1H-indole (**4r**):[6f] yellow solid (201 mg, 70% yield); mp 119–121 °C (lit.[6f] mp 121–122 °C); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.68 (s, 1H), 7.40–7.41 (m, 2H), 7.32–7.35 (m, 1H), 7.28 (s, 1H), 7.18–7.22 (m, 6H), 6.92–6.93 (m, 2H), 6.76 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 162.2 (d, J_{C-F} = 247.2 Hz), 139.8, 139.0, 138.4, 130.7 (d, J_{C-F} = 8.0 Hz) (2C), 129.5 (2C), 128.8 (d, J_{C-F} = 2.8 Hz), 128.3, 128.2 (2C), 127.5, 122.5, 120.9, 120.6, 115.4 (d, J_{C-F} = 21.4 Hz) (2C), 110.8, 103.7.

1-Phenyl-2-(p-tolyl)-1H-indole (**4s**): pale yellow solid (241 mg, 85% yield); mp 130–132 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.66–7.68 (m, 1H), 7.38–7.41 (m, 2H), 7.31–7.34 (m, 1H), 7.23–7.28 (m, 3H), 7.14–7.17 (m, 4H), 7.02–7.05 (m, 2H), 6.76 (s, 1H), 2.29 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 141.0, 139.0, 138.7, 137.2, 129.7, 129.4 (2C), 129.0 (2C), 128.9 (2C), 128.4, 128.2 (2C), 127.3, 122.3, 120.8, 120.5, 110.7, 103.4, 21.3; HRMS (ESI) calcd for $C_{21}H_{18}N$ (M + H$^+$) 284.1434, found 284.1441.

2-Cyclopropyl-1-phenyl-1H-indole (**4t**): yellow oil (149 mg, 64% yield); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.53–7.55 (m, 1H), 7.48–7.51 (m, 2H), 7.41–7.45 (m, 2H), 7.38–7.41 (m, 1H), 7.07–7.14 (m, 3H), 6.19 (s, 1H), 1.67–1.68 (m, 1H), 0.82–0.86 (m, 2H), 0.75–0.79 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 144.1, 138.2, 129.4 (2C), 128.18, 128.17 (2C), 128.06, 127.6, 121.2, 120.2, 119.9, 110.0, 97.4, 8.49, 8.46 (2C); HRMS (ESI) calcd for $C_{17}H_{16}N$ (M + H$^+$) 234.1277, found 234.1286.

2-(tert-Butyl)-1-phenyl-1H-indole (**4u**): yellow oil (152 mg, 61% yield); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.57 (d, J = 7.8 Hz, 1H), 7.47–7.49 (m, 3H), 7.36–7.37 (m, 2H), 7.06–7.09 (m, 1H), 7.00–7.03 (m, 1H), 6.64 (d, J = 8.2 Hz, 1H), 6.47 (s, 1H), 1.25 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 150.7, 140.9, 132.3, 130.9 (2C), 129.5, 129.1 (2C), 128.7, 121.2, 119.9, 119.7, 110.3, 99.3, 33.4, 31.1 (3C); HRMS (ESI) calcd for $C_{18}H_{20}N$ (M + H$^+$) 250.1590, found 250.1596.

2-(2-Bromophenyl)-1-phenyl-1H-indole (**4v**): yellow oil (268 mg, 77% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70–7.72 (m, 1H), 7.52 (d, J = 7.8 Hz, 1H), 7.29–7.36 (m, 3H), 7.18–7.25 (m, 7H), 7.09–7.13 (m, 1H), 6.75 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.0, 138.0, 137.8, 134.3, 133.1, 132.9, 129.7, 129.0 (2C), 128.0, 127.8 (2C), 127.1, 126.9, 124.8, 122.6, 121.0, 120.8, 110.8, 105.3; HRMS (ESI) calcd for $C_{20}H_{15}{}^{81}BrN$ (M + H$^+$) 350.0367, found 350.0368.

2-(2-Bromophenyl)-1-(p-tolyl)-1H-indole (**4w**): yellow oil (293 mg, 81% yield); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.70–7.72 (m, 1H), 7.49–7.52 (m, 1H), 7.33–7.35 (m, 1H), 7.23–7.26 (m, 1H), 7.08–7.20 (m, 8H), 6.73–6.75 (m, 1H), 2.30 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 139.1, 137.9, 136.9, 135.4, 134.4, 133.1, 132.9, 129.67 (2C), 129.63, 128.0, 127.6 (2C), 126.8, 124.8, 122.5, 120.9, 120.7, 110.9, 105.0, 21.2; HRMS (ESI) calcd for $C_{21}H_{17}{}^{81}BrN$ (M + H$^+$) 364.0524, found 364.0528.

2-(2-Bromophenyl)-1-(o-tolyl)-1H-indole (4x): yellow oil (225 mg, 62% yield); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.72−7.74 (m, 1H), 7.57 (d, *J* = 7.8 Hz, 1H), 7.22−7.24 (m, 3H), 7.17−7.20 (m, 3H), 7.07−7.13 (m, 3H), 6.95−6.96 (m, 1H), 6.84 (s, 1H), 1.99 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 139.1, 137.9, 136.9, 136.7, 133.8, 133.2, 132.7, 131.1, 129.8, 129.4, 128.3, 127.7, 126.6, 126.5, 124.5, 122.5, 120.9, 120.5, 111.1, 105.2, 18.1; HRMS (ESI) calcd for $C_{21}H_{17}{}^{81}BrN$ (M + H$^+$) 364.0524, found 364.0532.

2-(2-Bromophenyl)-1-(4-propylphenyl)-1H-indole (4y): yellow oil (285 mg, 73% yield); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.70−7.71 (m, 1H), 7.54 (d, *J* = 8.0 Hz, 1H), 7.35−7.36 (m, 1H), 7.23 (s, 1H), 7.17−7.20 (m, 3H), 7.11−7.13 (m, 5H), 6.74 (s, 1H), 2.56 (t, *J* = 7.4 Hz, 2H), 1.60−1.64 (m, 2H), 0.91 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 141.6, 139.1, 137.9, 135.5, 134.3, 133.1, 132.9, 129.6, 129.0 (2C), 127.9, 127.5 (2C), 126.8, 124.8, 122.5, 120.9, 120.6, 110.9, 105.0, 37.7, 24.4, 13.9; HRMS (ESI) calcd for $C_{23}H_{21}{}^{81}BrN$ (M + H$^+$) 392.0837, found 392.0848.

2-(2-Bromophenyl)-1-(4-chlorophenyl)-1H-indole (4z): white solid (241 mg, 63% yield); 127−130 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.70−7.73 (m, 1H), 7.53−7.55 (m, 1H), 7.32−7.33 (m, 1H), 7.26−7.30 (m, 3H), 7.20−7.25 (m, 3H), 7.16−7.17 (m, 3H), 6.76 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 138.9, 137.6, 136.6, 133.9, 133.1, 133.0, 132.7, 130.0, 129.3 (2C), 128.9 (2C), 128.1, 127.1, 124.8, 122.9, 121.1, 121.0, 110.5, 105.6; HRMS (ESI) calcd for $C_{20}H_{14}{}^{81}BrClN$ (M + H$^+$) 383.9978, found 383.9987.

Intermediate N-phenyl-2-(phenylethynyl)aniline (3a):[25] yellow oil (189 mg, 70% yield); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.51−7.53 (m, 2H), 7.46−7.48 (m, 1H), 7.31−7.36 (m, 5H), 7.24−7.26 (m, 1H), 7.19−7.21 (m, 3H), 7.03 (t, *J* = 7.4 Hz, 1H), 6.80−6.83 (m, 1H), 6.51 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 145.0, 141.8, 132.7, 131.6 (2C), 129.6, 129.5 (2C), 128.56 (2C), 128.55, 123.2, 122.7, 120.4 (2C), 119.3, 113.6, 110.3, 95.7, 85.8.

General Procedure for Pd-Catalyzed Synthesis of Indolo[1,2-*f*]-phenanthridine 5. An oven-dried Schlenk tube was charged with a magnetic stir bar, brominated 1,2-diphenyl-1*H*-indole **4** (0.5 mmol, 1 equiv), $Pd(OAc)_2$ (0.025 mmol, 5 mol %), P(*p*-Tol)$_3$ (0.05 mmol, 10 mol %), and Cs_2CO_3 (0.6 mmol, 1.2 equiv). The tube was capped and then evacuated and backfilled with nitrogen (3 times). Under a positive pressure of nitrogen, toluene (3 mL) was added via syringe. The tube was sealed and allowed to stir at 110 °C (monitored by TLC). After being cooled to room temperature, the mixture was diluted with ethyl acetate (30 mL), filtered through a plug of silica gel, and concentrated. The residue was purified by column chromatography on silica gel using petroleum ether/EtOAc (20:1 → 10:1, v:v) as eluent to give product **5**.

General Procedure for One-Pot Synthesis of Indolo[1,2-*f*]-phenanthridine 5. An oven-dried Schlenk tube was charged with a magnetic stir bar, 2-alkynylaniline **1** (0.3 mmol, 1 equiv), boronic acid **2** (0.45 mmol, 1.5 equiv), $Cu(OAc)_2$ (0.03 mmol, 10 mol %), and decanoic acid (0.06 mmol, 20 mol %). A solution of 2,6-lutidine (0.33 mmol, 1.1 equiv) in toluene (3 mL) was added via syringe. The tube was sealed and allowed to stir at room temperature for about 8 h (monitored by TLC) and then stir at 120 °C for 22−32 h. After the solution was cooled to room temperature, $Pd(OAc)_2$ (0.03 mmol, 10 mol %), P(*p*-Tol)$_3$ (0.06 mmol, 20 mol %), and Cs_2CO_3 (0.36 mmol, 1.2 equiv) were added under positive nitrogen atmosphere. After being filled with a positive nitrogen stream (for about 3 min), the tube was sealed and allowed to stir at 110 °C for 12−15 h (monitored by TLC). After being cooled to room temperature, the mixture was diluted with ethyl acetate (30 mL), filtered through a plug of silica gel, and concentrated. The residue was purified by column chromatography on silica gel using petroleum ether/EtOAc (20:1 → 10:1, v/v) as eluent to give product **5**.

Indolo[1,2-f]phenanthridine (5a):[10] white solid (115 mg, 86% yield); mp 140−141 °C (lit.[10] mp 140−142 °C); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.48 (d, *J* = 8.4 Hz, 1H), 8.34 (d, *J* = 8.4 Hz, 1H), 8.25 (d, *J* = 7.8 Hz, 1H), 8.14−8.16 (m, 1H), 8.06−8.08 (m, 1H), 7.81 (d, *J* = 7.6 Hz, 1H), 7.52 (t, *J* = 7.4 Hz, 1H), 7.41−7.45 (m, 2H), 7.29−7.36 (m, 3H), 7.21 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 136.1, 135.4, 134.0, 130.5, 128.9, 128.3, 128.0, 127.0, 126.3, 124.3, 124.2, 123.2, 122.6, 122.2, 122.17, 121.9, 121.2, 116.5, 114.4, 96.3.

6-Methylindolo[1,2-f]phenanthridine (5b): white solid (117 mg, 83% yield); mp 165−167 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.34 (d, *J* = 8.4 Hz, 1H), 8.30 (d, *J* = 8.4 Hz, 1H), 8.14−8.15 (m, 1H), 8.06−8.08 (m, 1H), 8.02 (s, 1H), 7.81 (d, *J* = 7.4 Hz, 1H), 7.40−7.45 (m, 2H), 7.29−7.36 (m, 3H), 7.20 (s, 1H), 2.44 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 135.3, 134.0, 133.9, 132.6, 130.4, 129.8, 128.2, 127.9, 127.0, 126.4, 124.4, 124.3, 122.6, 122.1, 122.0, 121.7, 121.2, 116.4, 114.3, 96.0, 21.3; HRMS (ESI) calcd for $C_{21}H_{16}N$ (M + H$^+$) 282.1277, found 282.1281.

8-Methylindolo[1,2-f]phenanthridine (5c): white solid (111 mg, 79% yield); mp 143−145 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.14 (d, *J* = 7.5 Hz, 1H), 8.07 (t, *J* = 7.5 Hz, 2H), 7.76−7.79 (m, 1H), 7.46−7.49 (m, 1H), 7.40−7.44 (m, 2H), 7.35−7.36 (m, 1H), 7.31(t, *J* = 7.6 Hz, 1H), 7.25−7.28 (m, 2H), 7.20 (s, 1H), 2.41 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 136.7, 135.8, 133.4, 131.9, 129.7, 128.3, 127.9, 127.7, 127.2, 126.5, 124.9, 123.9, 123.7, 122.8, 121.5, 120.74, 120.69, 120.62, 115.1, 97.4, 22.4; HRMS (ESI) calcd for $C_{21}H_{16}N$ (M + H$^+$) 282.1277, found 282.1278.

6-Propylindolo[1,2-f]phenanthridine (5d): white solid (125 mg, 81% yield); mp 191−192 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.31−8.33 (m, 1H), 8.28 (d, *J* = 8.2 Hz, 1H), 8.10−8.12 (m, 1H), 7.99−8.02 (m, 2H), 7.78 (d, *J* = 7.6 Hz, 1H), 7.36−7.39 (m, 2H), 7.29−7.35 (m, 2H), 7.26−7.27 (m, 1H), 7.14 (s, 1H), 2.65 (t, *J* = 7.6 Hz, 2H), 1.67−1.73 (m, 2H), 0.98 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 137.2, 135.2, 134.1, 133.8, 130.3, 129.0, 128.0, 127.7, 127.0, 126.2, 124.2, 123.7, 122.4, 121.92, 121.90, 121.6, 121.0, 116.2, 114.2, 95.9, 37.7, 24.8, 14.0; HRMS (ESI) calcd for $C_{23}H_{20}N$ (M + H$^+$) 310.1590, found 310.1596.

6-Chloroindolo[1,2-f]phenanthridine (5e): yellow solid (115 mg, 76% yield); mp 177−179 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.31 (d, *J* = 8.8 Hz, 1H), 8.19 (d, *J* = 8.0 Hz, 1H), 8.12 (d, *J* = 2.2 Hz, 1H), 8.02 (t, *J* = 7.8 Hz, 2H), 7.79 (d, *J* = 7.0 Hz, 1H), 7.41−7.47 (m, 3H), 7.32−7.37 (m, 2H), 7.16 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 135.0, 134.5, 133.9, 130.4, 129.0, 128.6, 128.5, 128.1, 126.5, 125.8, 124.3, 124.0, 123.9, 122.6, 122.5, 122.2, 121.4, 117.6, 114.1, 96.8; HRMS (ESI) calcd for $C_{20}H_{13}ClN$ (M + H$^+$) 302.0731, found 302.0737.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^{1}H and ^{13}C NMR spectra for the products. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Authors

*E-mail: wangxiaoxia@zjnu.cn.
*E-mail: lvxin@zjnu.cn.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We are grateful to the National Natural Science Foundation of China (No. 21202152) and the Zhejiang Provincial Natural Science Foundation (No. Y4110044) for financial support. We also thank Prof. Weiliang Bao for his suggestions and helping provide characterization of several compounds.

■ REFERENCES

(1) For selected reviews, see: (a) Kochanowska-Karamyan, A. J.; Hamann, M. T. *Chem. Rev.* **2010**, *110*, 4489−4497. (b) Somei, M.; Yamada, F. *Nat. Prod. Rep.* **2004**, *21*, 278−311. (c) *Indoles*; Sundberg, R. J., Ed.; Academic Press: London, 1996. (d) Brown, R. K. In *Indoles*; Houlihan, W. J., Ed.; Wiley-Interscience: New York, 1972.

(2) For selected reviews on indole synthesis, see: (a) Taber, D. F.; Tirunahari, P. K. *Tetrahedron* **2011**, *67*, 7195−7210. (b) Barluenga, J.; Rodriguez, F.; Fananas, F. J. *Chem.—Asian J.* **2009**, *4*, 1036−1048. (c) Kruger, K.; Tillack, A.; Beller, M. *Adv. Synth. Catal.* **2008**, *350*, 2153−2167. (d) Humphrey, G. R.; Kuethe, J. T. *Chem. Rev.* **2006**, *106*,

2875–2911. (e) Cacchi, S.; Fabrizi, G. *Chem. Rev.* **2005**, *105*, 2873–2920. (f) Zeni, G.; Larock, R. C. *Chem. Rev.* **2004**, *104*, 2285–2309. (g) Gribbe, G. W. *J. Chem. Soc., Perkin Trans. 1* **2000**, 1045–1075.

(3) For selected examples, see: (a) Yang, D. Z.; Wang, P.; Liu, J. Z.; Xing, H. L.; Liu, Y.; Xie, W. C.; Zhao, G. S. *Bioorg. Med. Chem.* **2014**, *22*, 1850–1862. (b) Sindac, J. A.; Barraza, S. J.; Dobry, C. J.; Xiang, J.; Blakely, P. K.; Irani, D. N.; Keep, R. F.; Miller, D. J.; Larsen, S. D. *J. Med. Chem.* **2013**, *56*, 9222–9241. (c) Jennings, L. D.; Foreman, K. W.; Rush, T. S., III; Tsao, D. H. H.; Mosyak, L.; Kincaid, S. L.; Sukhdeo, M. N.; Sutherland, A. G.; Ding, W.; Kenny, C. H.; Sabus, C. L.; Liu, H.; Dushin, E. G.; Moghazeh, S. L.; Labthavikul, P.; Petersen, P. J.; Tuckman, M.; Ruzin, A. V. *Bioorg. Med. Chem.* **2004**, *12*, 5115–5131. (d) Matter, H.; Defossa, E.; Heinelt, U.; Blohm, P.-M.; Schneider, D.; Muller, A.; Herok, S.; Schreuder, H.; Liesum, A.; Brachvogel, V.; Lonze, P.; Walser, A.; Al-Obeidi, F.; Wildgoose, P. *J. Med. Chem.* **2002**, *45*, 2749–2769. (e) Tarzia, G.; Diamantini, G.; Giacomo, B. D.; Spadoni, G. *J. Med. Chem.* **1997**, *40*, 2003–2010.

(4) For selected recent examples, see: (a) An, X.-L.; Chen, J.-R.; Li, C.-F.; Zhang, F.-G.; Zou, Y.-Q.; Guo, Y.-C.; Xiao, W.-J. *Chem.—Asian J.* **2010**, *5*, 2258–2265. (b) Facoetti, D.; Abbiati, G.; Eur, E. R. *J. Org. Chem.* **2009**, *74*, 2872–2882. (c) Abbiati, G.; Casoni, A.; Canevari, V.; Nava, D.; Rossi, E. *Org. Lett.* **2006**, *8*, 4839–4842. (d) Antilla, J. C.; Klapars, A.; Buchwald, S. L. *J. Am. Chem. Soc.* **2002**, *124*, 11684–11688. (e) Klapars, A.; Antilla, J. C.; Huang, X. H.; Buchwald, S. L. *J. Am. Chem. Soc.* **2001**, *123*, 7727–7729.

(5) For selected recent examples, see: (a) Chen, Z. Y.; Zheng, D. Q.; Wu, J. *Org. Lett.* **2011**, *13*, 848–851. (b) Zhou, H. W.; Zhu, D.; Xing, Y. P.; Huang, H. F. *Adv. Synth. Catal.* **2010**, *352*, 2127–2131. (c) Isono, N.; Lautens, M. *Org. Lett.* **2009**, *11*, 1329–1331. (d) Shen, Z. M.; Lu, X. Y. *Adv. Synth. Catal.* **2009**, *351*, 3107–3112. (e) Sakai, N.; Annaka, K.; Fujita, A.; Sato, A.; Konakahara, T. *J. Org. Chem.* **2008**, *73*, 4160–4165. (f) Tang, S.; Xie, Y.-X.; Li, J.-H.; Wang, N.-X. *Synthesis* **2007**, 1841–1847. (g) Nakamura, M.; Ilies, L.; Otsubo, S.; Nakamura, E. *Org. Lett.* **2006**, *8*, 2803–2805. (h) Hiroya, K.; Itoh, S.; Sakamoto, T. *J. Org. Chem.* **2004**, *69*, 1126–1136. (i) Hiroya, K.; Itoh, S.; Ozawa, M.; Kanamori, Y.; Sakamoto, T. *Tetrahedron Lett.* **2002**, *43*, 1277–1280.

(6) For a recent review about the domino C–N/C–C coupling reactions of *o*-*gem*-dihalovinylanilines, see: (a) Chelucchi, G. *Chem. Rev.* **2012**, *112*, 1344–1362 and references cited therein. For selected examples, see: (b) Fang, Y.-Q.; Lautens, M. *J. Org. Chem.* **2008**, *73*, 538–549. (c) Nagamochi, M.; Fang, Y.-Q.; Lautens, M. *Org. Lett.* **2007**, *9*, 2955–2958. (d) Fang, Y.-Q.; Yuen, J.; Lautens, M. *J. Org. Chem.* **2007**, *72*, 5152–5160. (e) Fayol, A.; Fang, Y.-Q.; Lautens, M. *Org. Lett.* **2006**, *8*, 4203–4206. (f) Fang, Y.-Q.; Lautens, M. *Org. Lett.* **2005**, *7*, 3549–3552. For these protocols, *N*-substituted *o*-*gem*-dihalovinylaniline substrates should be pre-synthesized from *o*-nitro aromatic aldehydes/ketones (generally in three steps).

(7) For selected examples, see: (a) Breazzano, S. P.; Poudel, Y. B.; Boger, D. L. *J. Am. Chem. Soc.* **2013**, *135*, 1600–1606. (b) Phetrak, N.; Rukkijakan, T.; Sirijaraensre, J.; Prabpai, S.; Kongsaeree, P.; Klinchan, C.; Chuawong, P. *J. Org. Chem.* **2013**, *78*, 12703–12709. (c) Goswami, K.; Duttagupta, I.; Sinha, S. *J. Org. Chem.* **2012**, *77*, 7081–7085. (d) Zhou, H.; Liao, X. B.; Cook, J. M. *Org. Lett.* **2004**, *6*, 249–252. (e) Larock, R. C.; Yum, E. K.; Fefvik, M. D. *J. Org. Chem.* **1998**, *63*, 7652–7662. (f) Larock, R. C.; Yum, E. K. *J. Am. Chem. Soc.* **1991**, *113*, 6690–6692.

(8) (a) Xu, M.; Xu, K.; Wang, S. Z.; Yao, Z.-J. *Tetrahedron Lett.* **2013**, *54*, 4675–4678. (b) Gimeno, A.; Medio-Simon, M.; de Arellano, C. R.; Asensio, G.; Cuenca, A. B. *Org. Lett.* **2010**, *12*, 1900–1903. (c) Murai, K.; Hayashi, S.; Takaichi, N.; Kita, Y.; Fujioka, H. *J. Org. Chem.* **2009**, *74*, 1418–1421. (d) Ye, S. Q.; Ding, Q. P.; Wang, Z. Y.; Zhou, H. B.; Wu, J. *Org. Biomol. Chem.* **2008**, *6*, 4406–4412. (e) Zhang, Y. H.; Donahue, J. P.; Li, C.-J. *Org. Lett.* **2007**, *9*, 627–630.

(9) For examples, see: (a) Yan, L. P.; Zhao, D. B.; Lan, J. B.; Cheng, Y. Y.; Guo, Q.; Li, X. Y.; Wu, N. J.; You, J. S. *Org. Biomol. Chem.* **2013**, *11*, 7966–7977. (b) Takeda, D.; Hirano, K.; Satoh, T.; Miura, M. *Heterocycl* **2012**, *86*, 487–496. (c) Lee, D. U.; Bae, J. S.; Nam, H.; Hong, S. G.; Lee, D. H.; Kim, S. S. Korean patent 2010113204. *Chem. Abstr.* **2010**, *153*, 618726.

(10) Baik, C.; Kim, D.; Kang, M.-S.; Song, K.; Kang, S. O.; Ko, J. *Tetrahedron* **2009**, *65*, 5302–5307.

(11) Xie, C. S.; Zhang, Y. H.; Huang, Z. D.; Xu, P. X. *J. Org. Chem.* **2007**, *72*, 5431–5434.

(12) For reports on the assembly of indolo[1,2-*f*]phenanthridines through Pd-catalyzed tandem N–H/C–H arylations of 2-arylindoles with *o*-dihaloarenes, see ref 9a,b. Only two indolo[1,2-*f*]phenanthridines were synthesized therein.

(13) For recent reviews, see: (a) Pellissier, H. *Chem. Rev.* **2013**, *113*, 442–524. (b) Liu, Y. Y.; Wan, J.-P. *Chem.—Asian J.* **2012**, *7*, 1488–1501. (c) Liu, Y. Y.; Wan, J.-P. *Org. Biomol. Chem.* **2011**, *9*, 6873–6894.

(14) For selected examples, see: (a) Zatolochnaya, O. V.; Gevorgyan, V. *Org. Lett.* **2013**, *15*, 2562–2565. (b) Lavery, C. B.; McDonald, R.; Stradiotto, M. *Chem. Commun.* **2012**, *48*, 7277–7279. (c) Ackermann, L.; Barfuber, S.; Potukuchi, H. K. *Adv. Synth. Catal.* **2009**, *351*, 1064–1072. (d) Ackermann, L.; Sandmann, R.; Kondrashov, M. V. *Synlett* **2009**, 1219–1222. (e) Tang, Z.-Y.; Hu, Q.-S. *Adv. Synth. Catal.* **2006**, *348*, 846–850. (f) Ackermann, L. *Org. Lett.* **2005**, *7*, 439–442. (g) Siebeneicher, H.; Bytschkov, I.; Doye, S. *Angew. Chem., Int. Ed.* **2003**, *42*, 3042–3044.

(15) Oda, Y.; Hirano, K.; Satoh, T.; Miura, M. *Org. Lett.* **2012**, *14*, 664–667.

(16) Yang, M.; Tang, J.; Fan, R. H. *Chem. Commun.* **2012**, *48*, 11775–11777.

(17) For a recent review about Chan–Lam coupling, see: (a) Rao, K. S.; Wu, T.-S. *Tetrahedron* **2012**, *68*, 7735–7754. For selected examples, see: (b) Gonzalez, I.; Mosquera, J.; Guerrero, C.; Rodriguez, R.; Cruces, J. *Org. Lett.* **2009**, *11*, 1677–1680. (c) Antilla, J. C.; Buchwald, S. L. *Org. Lett.* **2001**, *3*, 2077–2079. (d) Lam, Y. S. P.; Vincent, G.; Clark, C. G.; Deudon, S.; Jadhav, P. K. *Tetrahedron Lett.* **2001**, *42*, 3415–3418. (e) Collot, V.; Bovy, P. R.; Rault, S. *Tetrahedron Lett.* **2000**, *41*, 9053–9057. (f) Lam, P. Y. S.; Clark, C. G.; Saubern, S.; Adams, J.; Winters, M. P.; Chan, D. M. T.; Combs, A. *Tetrahedron Lett.* **1998**, *39*, 2941–2944. (g) Chan, D. M. T.; Monaca, K. L.; Wanag, R.-P.; Winters, M. P. *Tetrahedron Lett.* **1998**, *39*, 2933–2936.

(18) (a) Yuan, G. D.; Liu, H. Q.; Gao, J. L.; Xu, H. J.; Jiang, L.; Wang, X. X.; Lv, X. *RSC Adv.* **2014**, *4*, 21904–21908. (b) Gao, J. L.; Zhu, J. Y.; Chen, L. B.; Shao, Y. Y.; Zhu, J. Q.; Huang, Y. J.; Wang, X. X.; Lv, X. *Tetrahedron Lett.* **2014**, *55*, 3367–3373. (c) Yuan, G. D.; Liu, H. Q.; Gao, J. L.; Yang, K. J.; Niu, Q. S.; Mao, H.; Wang, X. X.; Lv, X. *J. Org. Chem.* **2014**, *79*, 1749–1757. (d) Niu, Q. S.; Mao, H.; Yuan, G. D.; Gao, J. L.; Liu, H. Q.; Tu, Y. W.; Wang, X. X.; Lv, X. *Adv. Synth. Catal.* **2013**, *355*, 1185–1192. (e) Xia, Z. M.; Wang, K.; Zheng, J. N.; Ma, Z. Y.; Jiang, Z. G.; Wang, X. X.; Lv, X. *Org. Biomol. Chem.* **2012**, *10*, 1602–1611.

(19) It was reported that decanoic acid acted as an excellent additive for the Cu(II)-catalyzed C–N coupling of anilines with arylboronic acids. For a representative example, see: Tzschucke, C. C.; Murphy, J. M.; Hartwig, J. F. *Org. Lett.* **2007**, *9*, 761–764.

(20) The positive effect of myristic acid for the Cu(II)-mediated amination of boronic acids was originally reported by Buchwald et al.; see ref 17c.

(21) (a) Ke, S.; Rachna, S.; Kathleen, J. R.; Tom, G. D. *Org. Lett.* **2009**, *11*, 3598–3601. (b) Akira, T.; Shin, K.; Yoshinori, Y. *J. Am. Chem. Soc.* **2000**, *122*, 5662–5663. (c) Kubiczak, G. A.; Oesch, F.; Borlakoglu, J. T.; Kunz, H.; Robertson, L. W. *J. Agric. Food Chem.* **1989**, *37*, 1160–1164. (d) Hirano, K.; Inaba, Y.; Watanabe, T.; Oishi, S.; Fujii, N.; Ohno, H. *Adv. Synth. Catal.* **2010**, *352*, 368–372.

(22) Kaspar, L. T.; Ackermann, L. *Tetrahedron* **2005**, *61*, 11311–11316.

(23) Barluenga, J.; Jimenez-Aquino, A.; Aznar, F.; Valdes, C. *Chem.—Eur. J.* **2010**, *16*, 11707–11711.

(24) Barluenga, J.; Jimenez-Aquino, A.; Aznar, F.; Valdes, C. *J. Am. Chem. Soc.* **2009**, *131*, 4031–4041.

(25) Park, J. H.; Kim, E.; Chung, Y. K. *Org. Lett.* **2008**, *10*, 4719–4721.