

A practical Cu(I)-catalyzed domino approach to 1,2-disubstituted indoles and its application for the assembly of indolophenanthridines

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Abstract

A facile and efficient approach to 1,2-disubstituted indoles has been developed using a novel Cu(I)-catalyzed cascade coupling/cyclization reaction of 2-alkynylanilines with aryl iodides. Facilitated by CuI/*t*-BuOK without any ligand or CuI/Cs₂CO₃/1,10-phenanthroline, a variety of 1,2-disubstituted indoles were conveniently generated in one pot with good to excellent yields. Furthermore, a series of indolo[1,2-*f*]phenanthridines were successfully assembled from the tandem reactions of 2-alkynylanilines with *o*-dihaloarenes through copper-catalyzed coupling / cyclization followed by palladium-catalyzed intramolecular direct C(*sp*²)-H arylation.

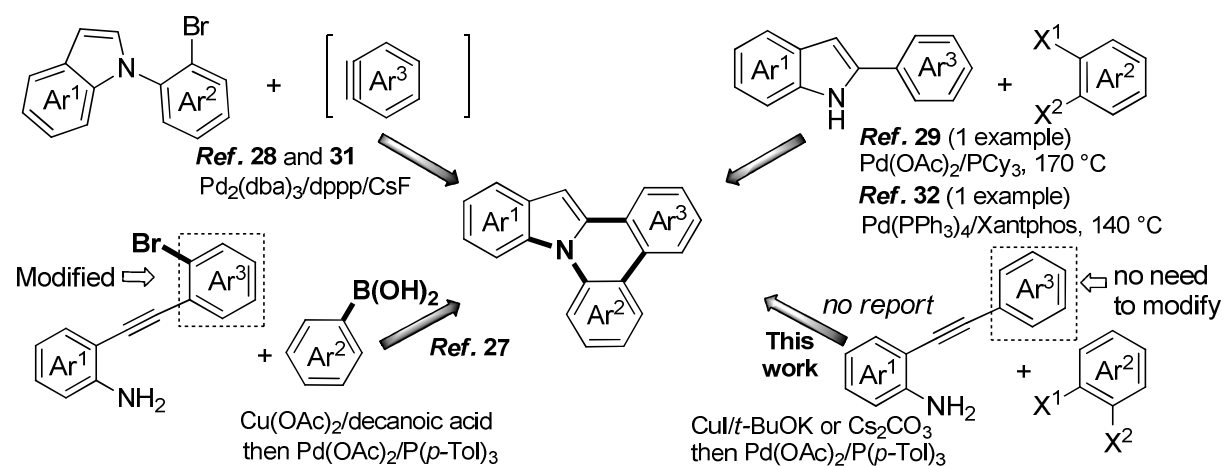
Keywords: Copper, cross-coupling, domino reactions, indoles, fused phenanthridines

Introduction

Many 1,2-disubstituted indoles are biologically active and pharmaceutically useful.^{1,2} The assembly of 1,2-disubstituted indoles have attracted great interest for their important applications in medicinal chemistry and materials science.^{3,4} Popular approaches to these heterocycles include N-modification of 2-substituted NH indoles,⁵⁻⁷ 2-arylation of N-substituted indoles,⁸⁻¹⁰ coupling/annulation of *o*-haloanilines with alkynes,¹¹⁻¹³ and intramolecular cyclization of *o*-(*gem*-dihalovinyl)anilines.¹⁴⁻¹⁶ Several one-pot synthetic protocols have also been developed recently.¹⁷⁻¹⁹ In spite of these remarkable progresses, many of the previous methods require expensive and/or sensitive catalysts (such as Pd and Au salts) or special substrates such as 1- or 2-substituted indoles and *o*-(*gem*-dihalovinyl)anilines. The annulation of N-substituted 2-alkynylanilines²⁰⁻²² and the coupling/cyclization of 2-alkynyl halobenzenes with primary amines²³⁻²⁵ can also generate 1,2-disubstituted indoles. Katz's group utilized the tandem

substitution/cyclization to furnish 2-substituted N-arylindoles, but the protocol was limited to the reactions of 2-alkynylfluorobenzenes.²⁶ Our group has developed a Cu(II)-catalyzed domino synthesis of 1,2-disubstituted indoles using coupling/cyclization of *o*-alkynylanilines with aryl boronic acids.²⁷ Compared with aryl boronic acids, aryl halides are relatively cheap and more easily accessible. So replacing the arylating reagents by aryl halides for the transformation may prove to be both practical and economic.

As a class of polycyclic indole derivatives, indolo[1,2-*f*]phenanthridines may be applied as functional materials for dye-sensitized solar cells (DSSCs)²⁸ or organic light-emitting diodes (OLEDs).^{29,30} However, there are only a few reports of convenient syntheses of these useful polycyclic heteroarenes.²⁷⁻³² The previously reported methods may have the limitations such as the use of special materials (*e.g.* arynes, 2-arylindoles, N-(*o*-bromophenyl)indoles, or 2-(*o*-bromoaryl)-1-arylindoles), the requirements of harsh conditions (high temperatures) and/or the restricted scopes (Scheme 1).



Scheme 1. Reports on the one-pot synthesis of indolo[1,2-*f*]phenanthridines.

Cu-mediated cross-coupling has aroused increasing interest for its low cost and high efficiency.^{33,34} And Cu-mediated domino transformation has been applied as an attractive methodology since it can conveniently and efficiently construct various heterocyclic moieties.³⁵ For instance, Ackermann *et al.* found that 1,2-disubstituted indoles could be synthesized using Cu(I)-catalyzed coupling/cyclization of 2-alkynyl haloarenes with anilines.³⁶ To our knowledge, there is no report on the Cu-catalyzed domino assembly of 1,2-disubstituted indole derivatives from *o*-alkynylanilines and aryl halides. Furthermore, a one-pot approach to indolo[1,2-*f*]phenanthridines from *o*-alkynylanilines and 1,2-dihaloarenes has not been achieved until now.

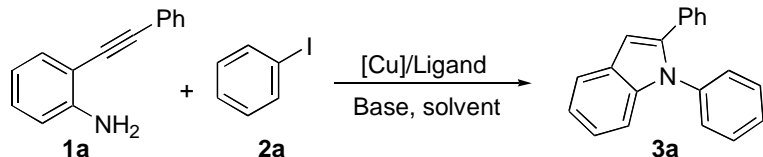
As part of our ongoing research efforts toward the domino synthesis of heterocycles under copper catalysis,^{27,37-40} we became interested in applying the one-pot protocol to the assembly of 1,2-disubstituted indoles and the tandem synthesis of indolo[1,2-*f*]phenanthridines. The findings are reported herein.

Results and Discussion

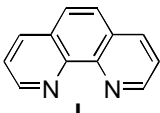
For a preliminary study we chose the reaction of 2-(phenylethynyl)aniline **1a** with iodobenzene **2a** as the model transformation. (Table 1) A good yield of the desired disubstituted indole **3a** was obtained when the reaction was performed with CuI (10 mol%), 1,10-phenanthroline (1,10-phen, 20 mol%), and Cs₂CO₃ (2 equiv) (entry 1). From the catalyst screen it was found that CuI was the best catalyst (compare entry 1 with entries 2-5). It was found that non-polar solvents performed better than polar ones, and toluene was chosen as the optimal solvent (compare entry 1 with entries 6-9). The study of the effect of ligands indicated that 1,10-phenanthroline was superior to others (compare entry 1 with entries 10-13). In a blank experiment 29% yield of the indole was obtained in the absence of any ligand (entry 14). Other bases were also tested, *t*-BuOK performing best (compare entry 18 with entries 1 and 15-17). The addition of ligand had little effect on the reaction when *t*-BuOK was used as the base (entries 18, 19). The amount of base could be reduced to 1.2 equiv without affecting the reaction efficiency (entry 20).

The scope of this Cu(I)-catalyzed domino protocol was then investigated using a wide range of 2-alkynylanilines and aryl halide (Table 2). Considering that milder conditions may be more compatible and favorable for some reactions, we also investigated several reactions with Cs₂CO₃ as the base (Table 2, **3a-3c**, **3e**, **3h**, **3i**, **3k**). In most cases, the performance of Cs₂CO₃ was comparable to that of *t*-BuOK (**3a-3c**, **3e**). However, when the alkynylanilines with functional groups (such as NO₂ and CF₃) were employed, the use of Cs₂CO₃ afforded the corresponding indoles in higher yields (**3h** and **3i**). Thus Cs₂CO₃ may be appropriate for the reactions of the substrates bearing strong electron-withdrawing groups. On the other hand, when other aryl halides (such as ArBr and ArCl) or *o*-alkynylanilines with bulky substituents (*e.g.* *t*-Bu and *o*-Br) were employed, *t*-BuOK was much more efficient than Cs₂CO₃ (**3a**, **3k** and **3l**).

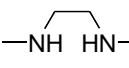
It is noteworthy that the reactions with *o*-dihaloarenes could selectively afford the desired N-(*o*-bromoaryl)indoles, which would provide an additional handle for further derivation of these products (Table 2, **3l-3q**). Inspired by the hypothesis that the intramolecular direct *sp*² C-H arylation of the N-(*o*-bromoaryl)indole would result in the formation of the corresponding polycyclic indole derivative, we attempted to synthesize the indolo[1,2-*f*]phenanthridine from 1-(2-bromophenyl)-2-phenyl-1*H*-indole (**3l**) by using this type of intramolecular transformation. Gratifyingly, the desired indolo[1,2-*f*]phenanthridine **4a** was smoothly generated under Pd-catalysis (Scheme 2). We then applied this protocol to the assembly of more indolo[1,2-*f*]phenanthridines from N-(*o*-bromoaryl)-2-arylindoles. The intramolecular C-H arylation of the indoles with different substituents (such as Me, *i*-Pr, Cl, and F) on the phenyls was also successfully achieved under Pd catalysis (Scheme 2).

Table 1. Optimization of the reaction conditions^a


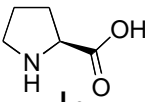
Ligands



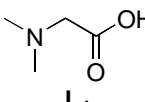
L₁



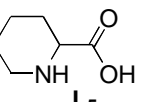
L₂



L₃



L₄



L₅

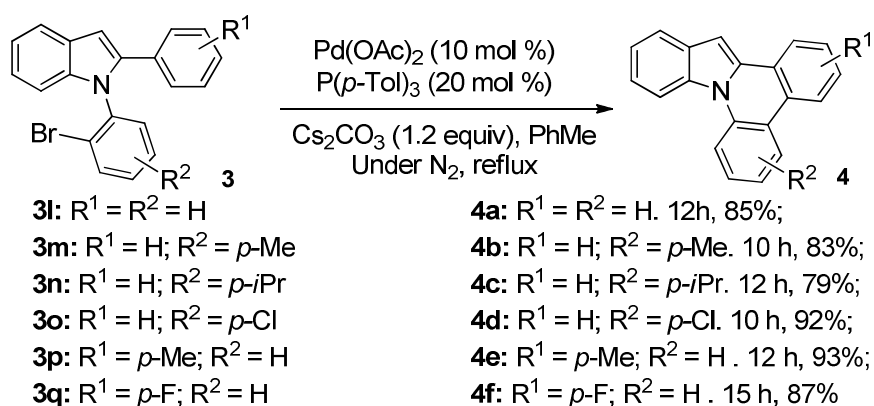
Entry	Catalyst	Ligand	Base	Solvent	Yield (%) ^b
1	CuI	L ₁	Cs ₂ CO ₃	toluene	85
2	CuBr	L ₁	Cs ₂ CO ₃	toluene	81
3	CuCl	L ₁	Cs ₂ CO ₃	toluene	78
4	Cu ₂ O	L ₁	Cs ₂ CO ₃	toluene	43
5	Cu(OAc) ₂	L ₁	Cs ₂ CO ₃	toluene	67
6	CuI	L ₁	Cs ₂ CO ₃	<i>o</i> -xylene	72
7	CuI	L ₁	Cs ₂ CO ₃	DCE	28
8	CuI	L ₁	Cs ₂ CO ₃	dioxane	45
9	CuI	L ₁	Cs ₂ CO ₃	DMF	21
10	CuI	L ₂	Cs ₂ CO ₃	toluene	37
11	CuI	L ₃	Cs ₂ CO ₃	toluene	31
12	CuI	L ₄	Cs ₂ CO ₃	toluene	25
13	CuI	L ₅	Cs ₂ CO ₃	toluene	43
14	CuI	- ^c	Cs ₂ CO ₃	toluene	29
15	CuI	L ₁	K ₂ CO ₃	toluene	33
16	CuI	L ₁	Na ₂ CO ₃	toluene	13
17	CuI	L ₁	K ₃ PO ₄	toluene	84
18	CuI	L ₁	<i>t</i> -BuOK	toluene	88
19	CuI	- ^c	<i>t</i> -BuOK	toluene	87
20	CuI	- ^c	<i>t</i> -BuOK ^d	toluene	87

^a Reaction conditions: 2-(phenylethynyl)aniline (1.0 mmol), iodobenzene (1.1 mmol), Cu catalyst (0.1 mmol, 10 mol%), ligand (0.2 mmol, 20 mol%), and base (2.0 equiv), in dry solvent (3 mL), under N₂, at 110 °C for 12 h. ^b Isolated yield (%). ^c No ligand. ^d 1.2 equiv of *t*-BuOK was utilized as the base.

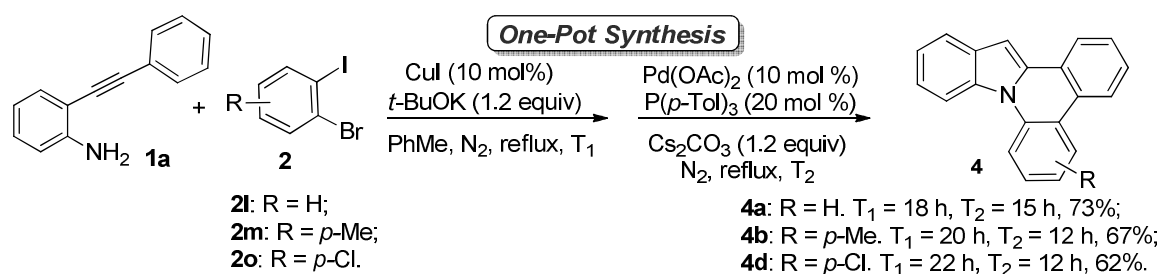
Table 2. Cu(I)-catalyzed domino synthesis of 1,2-disubstituted indoles

Indole 3	R ¹	R ²	Ar	Time (h)	Yield ^a %
3a	H	Ph	Ph	12	87 (85) ^b
3a				24	45 ^c (28) ^{b,c}
3a				24	12 ^d
3b	H	Ph	4-MeC ₆ H ₄	12	92 (86) ^b
3c	H	Ph	4-ClC ₆ H ₄	12	72 (67) ^b
3d	H	Ph	2-naphthyl	15	70
3e	5-Me	Ph	Ph	12	88 (82) ^b
3f	5-Cl	Ph	Ph	18	72
3g	H	4-FC ₆ H ₄	Ph	12	81
3h	H	4-O ₂ NC ₆ H ₄	Ph	20	51 (66) ^b
3i	H	4-F ₃ CC ₆ H ₄	Ph	20	49 (61) ^b
3j	H	cyclopropyl	Ph	22	70
3k	H	<i>t</i> -butyl	Ph	22	65 (28) ^b
3l	H	Ph	2-BrC ₆ H ₄	18	76 (63) ^b
3m	H	Ph	2-Br-4-MeC ₆ H ₃	20	71
3n	H	Ph	2-Br-4- <i>i</i> PrC ₆ H ₃	22	68
3o	H	Ph	2-Br-4-ClC ₆ H ₃	22	65
3p	H	4-MeC ₆ H ₄	2-BrC ₆ H ₄	18	67
3q	H	4-FC ₆ H ₄	2-BrC ₆ H ₄	22	52

^a Yield under conditions *a* unless otherwise indicated; ligand-free; ^b Conditions *b*; ^c Using PhBr instead of PhI as **2**; ^d Using PhCl instead of PhI as **2**.

**Scheme 2.** Pd-catalyzed synthesis of indolo[1,2-*f*]phenanthridines.

In order further to enhance the power and practicality of the method, we next tried to combine the above two steps in one pot. Fortunately, the one-pot tandem synthesis of the polycyclic indoles was also achieved (Scheme 3). Initially, the domino synthesis of **3l** was chosen as the model reaction. After stirring for 18 h under the Cu(I) catalysis, Pd(OAc)₂, P(*p*-Tol)₃ and Cs₂CO₃ were directly added to the reaction mixture without isolating intermediate **3l**. We were pleased to find that the desired indolo[1,2-*f*]phenanthridine **4a** was isolated in 85% yield (Scheme 3, entry 1). The domino reactions with other *o*-bromo iodobenzenes were also successively investigated, and moderate to good yields of the desired polycyclic heteroarenes were assembled. Compared with previous reports^{29,31,32}, the present methods provided a more convenient and versatile approach to these polycyclic heterocycles, and the starting materials were more easily accessible (see Scheme 1).

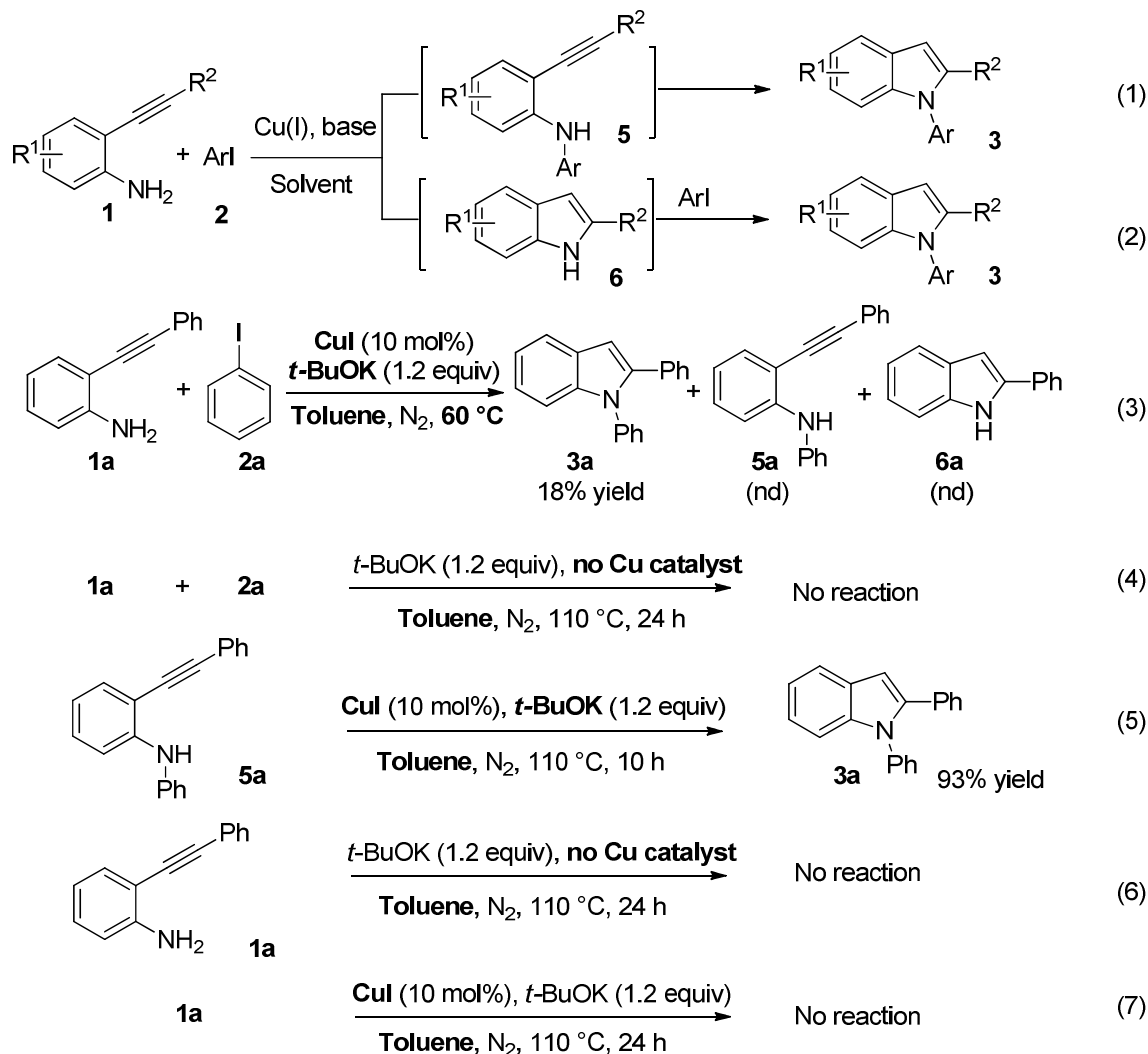


Scheme 3. One-pot synthesis of indolo[1,2-*f*]phenanthridines under sequential Cu/Pd catalysis.

Scheme 4 shows several control experiments that were carried out to obtain insight into the mechanism of the Cu(I)-catalyzed domino transformation. There are two possible routes to the formation of the 1,2-disubstituted indoles: (1) the intermolecular coupling / intramolecular cyclization process (Scheme 4, Eq. 1), and (2) the intramolecular cyclization / intermolecular coupling process (Eq. 2).⁴¹⁻⁴⁴

We attempted to capture the intermediate *N*-phenyl-2-(phenylethynyl)aniline **5a** or 2-phenylindole **6a** at a lower temperature (Eq. 3). However, only 18% of *N*-phenylindole **3a** was isolated in this case. Without the addition of any copper catalyst, neither the desired indole **3a** nor any intermediate was detected (Eq. 4), indicating that the copper catalyst was indispensable for the domino reaction. Notably, we also synthesized the intermediate **5a**²⁷ and then subjected it to the standard copper(I)-catalyzed conditions (Eq. 5). The intramolecular annulation efficiently occurred to afford the desired indole in excellent yield (Eq. 5), indicating that the reaction probably underwent a coupling/cyclization process. In order to further eliminate the possibility of the cyclization/coupling pathway under our conditions (Eq. 1), two additional control experiments were also performed. With or without the promotion of the Cu catalyst, no cyclized product **6a** was detected when iodobenzene was absent under the standard conditions (Eq. 6 and Eq. 7). It is worth noting that the weakly polar toluene was employed as the solvent in our transformation, and the results significantly differ from those methods⁴²⁻⁴⁴ using strongly polar

solvents.⁴⁵ Based on these experiments and the relevant reports,⁴⁶ we tend to the opinion that the domino transformation probably underwent the intermolecular C-N coupling / intramolecular cyclization pathway (Eq. 1).



Scheme 4. Control experiments to probe the possible pathway of the one-pot indole synthesis.

Conclusions

In summary, we have demonstrated a copper(I)-catalyzed domino synthesis of 1,2-disubstituted indoles from 2-alkynylanilines and aryl halides. A broad range of the readily available starting materials can be efficiently and easily converted into the desired 1,2-disubstituted indole derivatives under the low-cost copper catalysis. Furthermore, the Cu(I)-mediated domino reactions with *o*-bromoiodoarenes selectively afforded the corresponding N-(*o*-bromoaryl)-

indoles, which were further transformed to indolo[1,2-*f*]phenanthridine *via* Pd-catalyzed intramolecular direct C(*sp*²)-H arylation. The polycyclic indole derivatives were also smoothly assembled in one pot by sequential Cu/Pd catalysis. The high efficiency, the convenient procedures, and the wide application scope would make this protocol attractive for the assembly of heterocyclic molecules of biological or materials interest.

Experimental Section

General. Unless otherwise noted, all one-pot reactions were carried out in an oven-dried Schlenk tube equipped with a magnetic stir bar under N₂ atmosphere. Toluene, *o*-xylene and dioxane were distilled from Na; DCE and DMF were distilled from CaH₂. 2-alkynylanilines⁴⁷ and aryl halides⁴⁸ were synthesized according to the known literature. All other reagents were obtained from commercial sources and used without further purification, unless stated otherwise. The NMR spectra were recorded in CDCl₃ on a 600 MHz instrument with TMS as internal standard. Recorded shifts were reported in parts per million (δ) 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. TLC was carried out with 0.2 mm thick silica gel plates (GF254). Visualization was achieved by UV light. The columns were hand packed with silica gel 60 (150-200 mesh). Unknown products were additionally confirmed by HRMS. Mass spectra were obtained using ESI ionization.

General procedure for the Cu(I)-catalyzed one-pot synthesis of 1,2-disubstituted indoles 3 with *t*-BuOK as the base. An oven-dried Schlenk tube was charged with a magnetic stir bar, 2-alkynylaniline **1** (1.0 mmol, 1 equiv), CuI (0.1 mmol, 10 mol %) and *t*-BuOK (1.2 mmol, 1.2 equiv). The tube was capped and then evacuated and backfilled with nitrogen (3 times). Under a positive pressure of nitrogen, a solution of aryl halide (1.1 mmol, 1.1 equiv) in 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 petrol/EtOAc (50:1 \rightarrow 20:1 v/v) as eluent to give product **3**.

General procedure for the Cu(I)-catalyzed one-pot synthesis of 1,2-disubstituted indoles 3 with Cs₂CO₃ as the base. An oven-dried Schlenk tube was charged with a magnetic stir bar, 2-alkynylaniline **1** (1.0 mmol, 1 equiv), CuI (0.1 mmol, 10 mol %), 1,10-phen (0.2 mmol, 20 mol) and Cs₂CO₃ (2 mmol, 2 equiv). The tube was capped and then evacuated and backfilled with nitrogen (3 times). Under a positive pressure of nitrogen, a solution of aryl halide (1.1 mmol, 1.1 equiv) in 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 petrol/EtOAc (50:1 → 20:1 v/v) as eluent to give product **3**.

General procedure for the Pd-catalyzed synthesis of indolo[1,2-*f*]phenanthridines **4.** An oven-dried Schlenk tube was charged with a magnetic stir bar, brominated 1,2-diphenyl-1*H*-indole **3** (0.3 mmol, 1 equiv), Pd(OAc)₂ (0.03 mmol, 10 mol %), (*p*-Tol)₃P (0.06 mmol, 20 mol %) and Cs₂CO₃ (0.36 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 then added. 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 petrol/EtOAc (20:1 → 10:1 v/v) as eluent to give product **4**.

General procedure for the one-pot tandem synthesis of indolo[1,2-*f*]phenanthridine **4 under sequential Cu/Pd catalysis.** An oven-dried Schlenk tube was charged with a magnetic stir bar, 2-alkynylaniline **1** (1 mmol, 1 equiv), CuI (0.1 mmol, 10 mol %) and *t*-BuOK (1.2 mmol, 1.2 equiv). The tube was capped and then evacuated and backfilled with nitrogen (3 times). Under a positive pressure of nitrogen, a solution of *o*-bromiodobenzene **2** (1.1 mmol, 1.1 equiv) in 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, Pd(OAc)₂ (0.03 mmol, 10 mol %), (*p*-Tol)₃P (0.06 mmol, 20 mol %) and Cs₂CO₃ (0.36 mmol, 1.2 equiv) was added. Filled with positive nitrogen stream (3 minutes), 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 petrol/EtOAc (20:1 → 10:1 v/v) as eluent to give product **4**.

Selected spectral data of products **3**:

1,2-Diphenyl-1*H*-indole (3a).⁴⁹ White solid (87% yield); mp 78–79 °C (Lit. mp 78–80 °C). ¹H NMR (600 MHz, CDCl₃): δ 7.66–7.67 (m, 1H), 7.34–7.36 (m, 2H), 7.28–7.29 (m, 2H), 7.24–7.25 (m, 2H), 7.16–7.22 (m, 7H), 6.79 (s, 1H). ¹³C NMR (150 MHz, CDCl₃): δ 140.8, 139.1, 138.6, 132.6, 129.3 (2C), 129.0 (2C), 128.4, 128.3 (2C), 128.1 (2C), 127.4, 127.3, 122.5, 120.8, 120.7, 110.7, 103.8.

2-Phenyl-1-(*p*-tolyl)-1*H*-indole (3b).⁵⁰ Pale yellow solid (92% yield); mp 80–82 °C. ¹H NMR (600 MHz, CDCl₃): δ 7.67–7.69 (m, 1H), 7.20–7.29 (m, 8H), 7.15–7.18 (m, 2H), 7.12–7.14 (m, 2H), 6.79 (s, 1H), 2.40 (s, 3H). ¹³C NMR (150 MHz, CDCl₃): δ 140.9, 139.2, 137.2, 136.0, 132.8, 130.0 (2C), 129.0 (2C), 128.3 (2C), 128.27, 127.9 (2C), 127.4, 122.3, 120.7, 120.6, 110.8, 103.5, 21.3.

1-(4-Chlorophenyl)-2-phenyl-1*H*-indole (3c).⁵¹ Yellow solid (72% yield); mp 100–102 °C. ¹H NMR (600 MHz, CDCl₃): δ 7.67–7.68 (m, 1H), 7.36–7.38 (m, 2H), 7.23–7.28 (m, 6H), 7.16–7.19 (m, 4H), 6.80 (s, 1H). ¹³C NMR (150 MHz, CDCl₃): δ 140.7, 138.9, 137.2, 133.0, 132.3, 129.6 (2C), 129.31 (2C), 129.30, 129.1 (2C), 128.5 (2C), 127.6, 122.7, 121.1, 120.8, 110.5, 104.3.

1-(2-Bromophenyl)-2-phenyl-1H-indole (3l). Yellow oil (76% yield). ^1H NMR (600 MHz, CDCl_3): δ 7.68–7.70 (m, 2H), 7.29–7.32 (m, 3H), 7.17–7.25 (m, 7H), 6.96–6.98 (m, 1H), 6.82 (s, 1H). ^{13}C NMR (150 MHz, CDCl_3): δ 141.3, 138.9, 138.2, 133.8, 132.5, 131.5, 130.9, 129.9, 128.6 (2C), 128.5, 128.4 (2C), 127.6, 124.1, 122.5, 120.9, 120.7, 111.1, 103.5. HRMS (ESI) calcd. for $\text{C}_{20}\text{H}_{15}^{81}\text{BrN}$ ($\text{M} + \text{H}^+$): 350.0367; found: 350.0376.

1-(2-Bromo-4-methylphenyl)-2-phenyl-1H-indole (3m). Yellow oil (71% yield). ^1H NMR (600 MHz, CDCl_3): δ 7.68–7.70 (m, 1H), 7.51 (s, 1H), 7.31–7.32 (m, 2H), 7.21–7.25 (m, 3H), 7.15–7.17 (m, 2H), 7.12 (s, 2H), 6.95–6.97 (m, 1H), 6.81 (s, 1H), 2.37 (s, 3H). ^{13}C NMR (150 MHz, CDCl_3): δ 141.3, 140.2, 139.0, 135.4, 134.2, 132.6, 131.0, 129.3, 128.6 (2C), 128.3 (2C), 127.5, 123.7, 122.4, 120.8, 120.6, 111.1, 103.3, 21.0. HRMS (ESI) calcd. for $\text{C}_{21}\text{H}_{17}^{81}\text{BrN}$ ($\text{M} + \text{H}^+$): 364.0524; found: 364.0533.

Selected spectral data of products 4

Indolo[1,2-f]phenanthridine (4a).³¹ White solid (85% yield); mp 140–141 °C (Lit. mp: 140–142 °C). ^1H NMR (600 MHz, CDCl_3): δ 8.45 (d, J 8.3 Hz, 1H), 8.31 (d, J 8.2 Hz, 1H), 8.21 (d, J 7.6 Hz, 1H), 8.10–8.12 (m, 1H), 8.03–8.05 (m, 1H), 7.80 (d, J 7.2 Hz, 1H), 7.49 (t, J 8.3 Hz, 1H), 7.38–7.42 (m, 2H), 7.31–7.36 (m, 2H), 7.26 (t, J 7.6 Hz, 1H), 7.18 (s, 1H). ^{13}C NMR (150 MHz, CDCl_3): δ 136.1, 135.3, 134.0, 130.5, 128.8, 128.3, 127.9, 126.9, 126.2, 124.2, 124.1, 123.1, 122.5, 122.2, 122.1, 121.9, 121.2, 116.4, 114.4, 96.3.

6-Methylindolo[1,2-f]phenanthridine (4b). White solid (83% yield); mp 165–167 °C. ^1H NMR (600 MHz, CDCl_3): δ 8.42 (d, J 8.4 Hz, 1H), 8.35 (d, J 8.3 Hz, 1H), 8.21–8.22 (m, 1H), 8.12–8.14 (m, 1H), 8.10 (s, 1H), 7.83 (d, J 7.8 Hz, 1H), 7.46–7.49 (m, 2H), 7.36–7.38 (m, 2H), 7.33 (t, J 7.2 Hz, 1H), 7.24–7.25 (m, 1H), 2.50 (s, 3H). ^{13}C NMR (150 MHz, CDCl_3): δ 135.3, 134.0, 133.9, 132.5, 130.3, 129.6, 128.1, 127.8, 127.0, 126.3, 124.3, 124.2, 122.5, 122.01, 122.0, 121.7, 121.1, 116.2, 114.3, 96.0, 21.2. HRMS (ESI) calcd. for $\text{C}_{21}\text{H}_{16}\text{N}$ ($\text{M} + \text{H}^+$): 282.1277; found: 282.1281.

6-Chloroindolo[1,2-f]phenanthridine (4d). Yellow solid (92% yield), mp 177 - 179 °C. ^1H NMR (600 MHz, CDCl_3): δ 8.35 (d, J 8.8 Hz, 1H), 8.22 (d, J 8.0 Hz, 1H), 8.16 (s, 1H), 8.05 (m, 2H), 7.81 (d, J 7.2 Hz, 1H), 7.44 - 7.49 (m, 3H), 7.33 - 7.38 (m, 2H), 7.19 (s, 1H). ^{13}C NMR (150 MHz, CDCl_3): δ 134.9, 134.5, 133.8, 130.4, 128.9, 128.5, 128.46, 128.0, 126.4, 125.8, 124.2, 123.9, 123.8, 122.6, 122.4, 122.1, 121.3, 117.5, 114.1, 96.8. HRMS (ESI) calcd. for $\text{C}_{20}\text{H}_{13}\text{ClN}$ ($\text{M} + \text{H}^+$): 302.0731; found: 302.0737.

Supplementary Material available

Experimental procedures, characterization data (for all the products), copies of ^1H and ^{13}C NMR spectra associated with this paper can be found in the online version.

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solvent. The use of the weakly polar solvent might be unfavorable to the intramolecular cyclization process of substrate **1a** (Scheme 4, Eq. 6-7). Therefore, the intermolecular coupling between substrate **1a** and reagent **2a** may take priority (Scheme 4, eq 5). After the amino group was arylated, the enhanced acidity of aryl-NH might favor the intramolecular annulation.

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