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Copper-Mediated One-Pot Synthesis of Indoles through Sequential Hydroamination and Cross-Dehydrogenative Coupling Reaction

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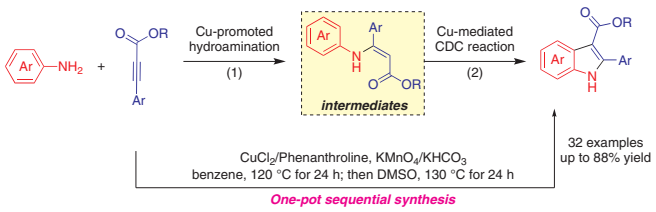

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Abstract Starting from simple anilines and ester arylpropiolates, an efficient one-pot synthesis of 2-arylindole-3-carboxylate derivatives has been developed through copper-mediated sequential hydroamination and cross-dehydrogenative coupling (CDC) reaction. The initial hydroamination of anilines to ester arylpropiolates in benzene can proceed in a stereoselective manner to give ester (*Z*)-3-(arylamino)acrylates in the presence of $CuCl_2$/phenanthroline, $KMnO_4$, and $KHCO_3$ at 120 °C. Sequentially, these in situ functionalized adducts can undergo direct intramolecular oxidative alkenylation of aromatic C–H bond in mixed solvents (benzene/DMSO 1:1) at 130 °C affording multi-substituted indoles in good to high yields.

Key words copper-mediated, indoles, hydroamination, cross-dehydrogenative coupling, oxidation

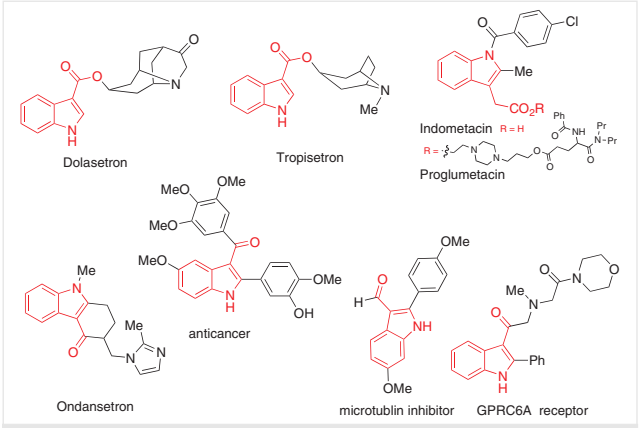

Figure 1 Selected examples of bioactive C3-functionalized indole derivatives

As one of the most abundant structural motifs, the indole unit has been widely found in biologically active natural products,[1] agrochemicals,[2] and pharmaceuticals.[3] Substituted indoles have been utilized as 'privileged scaffolds' for drug discovery;[4] numerous compounds display versatile biological activities such as anticancer, antifungal, antibacterial, anti-inflammatory, antioxidant, antirheumatoidal, and anti-HIV.[5] In particular, indole-3-carboxylic esters and 3-acylindoles are prevalent in a number of marketed drugs, such as Dolasetron (nausea), Tropisetron (antiemetic), Indomethacin/Proglumetacin (anti-inflammatory), and Ondansetron (nausea); and bioactive molecules (Figure 1). Therefore, C3-functionalized indole derivatives are of great interest for pharmaceutical and biological research.

The importance of the indole framework in drug discovery has pushed it to the forefront of synthetic developments. Over the past century, much effort has been focused on the development of new synthetic methods, and a large number of different approaches for indole preparation have been reported.[6] While classical procedures based on condensation and cyclization are well established,[6b] transition-metal-mediated C–C and C–N bond formation has recently emerged as an attractive alternative methodology for modular indole syntheses.[7] Specifically, reactions of alkynes and different nitrogen partners (such as aryl hydrazines,[8] aryl isonitriles,[9] nitroarenes,[10] diaziridinone,[11] and aniline derivatives[12–21]) set the stage for the development of practical approaches to diversely substituted indoles in the last few decades (Scheme 1).

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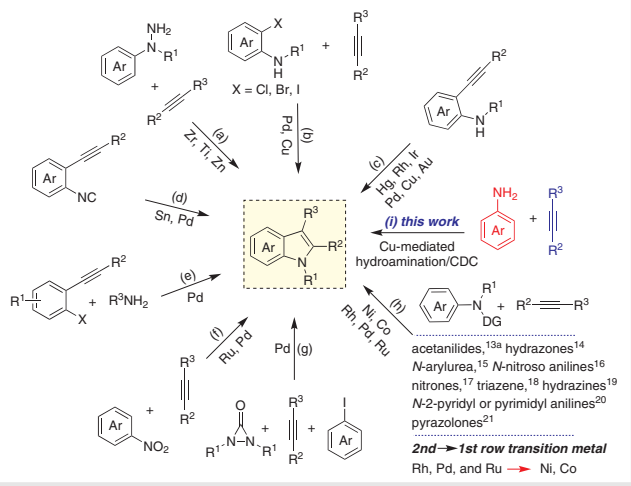


Scheme 1 Metal-mediated indole synthesis from alkynes and different nitrogen sources

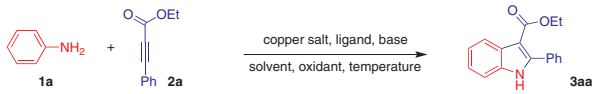
Due to improved atom and step economy, recent years have witnessed an upsurge in indole synthesis based on C–H activation processes. For example, since Glorius group[22a] reported an efficient synthesis of indoles via Pd-catalyzed oxidative cyclization of *N*-arylenaminones/esters in 2008, much effort has been focused on the development of intramolecular cross-dehydrogenative coupling (CDC) strategy.[23] In addition, various one-pot methods have also been well established through sequential addition/metal-catalyzed CDC reaction by Cacchi,[24] Fagnou,[13a,b] Jiao,[12a] and others.[12d,e] Using simple anilines[12] or aniline derivatives with diverse directing groups[13–21] (Scheme 1h), instead of *o*-haloanilines, *o*-alkynylanilines, *o*-alkynylaryl isocyanides, *o*-alkynylhaloarenes[25] and *o*-gem-dihalovinylanilines[26] as the substrates (Scheme 1b–e),[7] various metal-catalyzed protocols have been established through oxidative annulation of alkynes. Compared with Au/PhI(OAc)$_2$,[12e] Rh, Pd, and Ru catalysts, indole synthesis catalyzed by first-row transition metals is still very scarce. Despite Co-[15c,16c,17d,19b] or Ni-catalyzed[20d] indole synthesis through group-directed oxidative C–H annulation has been investigated in recent years, finding more available and cheaper first-row metals to synthesize indoles is still in great demand. As an alternative non-precious metal, copper-mediated C-heteroatom and C–C bond formation[27] through either traditional or C–H functionalization processes has aroused great interest in the synthesis of heterocycles.[28,29]

With our continuous efforts on metal-catalyzed (Cu[29n,30] and Pd[31]) C–H functionalization, herein we envisioned that simple anilines and alkynes should be suitable substrates for atom and step-economic synthesis of indoles through sequential copper-mediated hydroamination[32] and oxidative CDC reaction[22–24] (Scheme 1i). To realize this proposed tandem process, rational reaction conditions should be established to accommodate two fundamentally different copper-mediated reactions in one-pot manner.

With this consideration in mind, aniline (**1a**) and ethyl 3-phenylpropiolate (**2a**) were selected as the coupling partners to verify the above assumption. In the presence of CuCl$_2$ or CuI/2-(di-*tert*-butylphosphino)biphenyl (**L1**)[29n] and KHCO$_3$ as the base, the model reaction was initially conducted in a single solvent (MeCN, toluene, DCE, THF, 1,4-dioxane, DMF, DMA, and DMSO) at 120 or 130 ° for 24 hours with O$_2$ as the oxidant; however, no successful examples were obtained. Thus, based on these failed results, different solvent system was used to carry out hydroamination and CDC reaction, respectively. The optimization of reaction conditions are summarized in Table 1. First, a screen of copper salts [CuBr, CuCl, Cu(OTf)$_2$, Cu(OAc)$_2$, and CuCl$_2$] showed that CuCl and CuCl$_2$ gave a similar yield (12% vs 13%, Table 1, entries 3 and 6), whereas other copper salts led to lower yields (entries 1–6). It must be noted that the direct use of mixed solvents (MeCN/DMSO = 1:1) gave no product (entries 1 and 2). To increase the yield of **3aa**, the influence of ligands (phosphorus ligands **L1**–**L3**, *N*-heterocyclic carbene ligand **L4**, and nitrogen-based bidentate ligands **L5**–**L7**) on the reaction was then examined (entries 6–12). Bidentate nitrogen-containing ligand 1,10-phenanthroline (phen, **L7**) performed best, and the yield of **3aa** can be improved to 33% (entry 12). Next, the effect of bases such as KHCO$_3$, Li$_2$CO$_3$, NaO*t*-Bu, NaOMe, NaOAc, NaOH, Na$_2$CO$_3$, and NEt$_3$ on the reaction was investigated (entries 12–19). The nature of base greatly influenced the outcome of the reaction; KHCO$_3$ gave the best result with O$_2$ as the oxidant (entry 12). To reveal the crucial role of the oxidant, we then screened different types of oxidants (such as O$_2$, KMnO$_4$, 1,4-benzoquinone, K$_2$S$_2$O$_8$, MnO$_2$, and K$_2$Cr$_2$O$_7$, entries 20–24), and the yield was improved to 53% in the presence of KMnO$_4$ (entry 20). Finally, a survey of reaction media showed that benzene as the solvent for the hydroamination step provided better results than those obtained in MeCN, THF, DMF, toluene, DCE, and 1,4-dioxane (entries 20 and 25–30); furthermore, the binary mixed solvent composed of benzene and DMSO efficiently promoted the intramolecular CDC process at 130 °C to give the final product **3aa** in 88% yield (entry 30). A set of experiments were carried out to assess the crucial role of the amount of CuCl$_2$ (entry 31). When the amount was reduced to 50, 25 and 15 mmol%, the desired product was isolated in much lower yields.

Having established the feasibility of indole synthesis via copper-mediated sequential hydroamination/oxidative CDC process, we then explored the scope and limitation of anilines using ethyl 3-phenylpropiolate (**2a**) as the coupling partner (Table 2). As shown in Table 2, most of substituents (such as Me, OMe, F, Cl, and Br) on the aromatic moiety of anilines were applicable, and the corresponding indoles **3ba**–**la** were obtained in good to high yields (71–88%). Primary aromatic amines containing electron-donating groups at the *ortho*- (**1g** and **1h**), *meta*- (**1k** and **1l**), or *para*-position (**1b** and **1c**) were generally more reactive than those bearing electron-withdrawing substituents (**1d**–**f**, and **1i**)

Table 1 Optimization of Reaction Conditions for the Synthesis of Indole **3aa**[a]



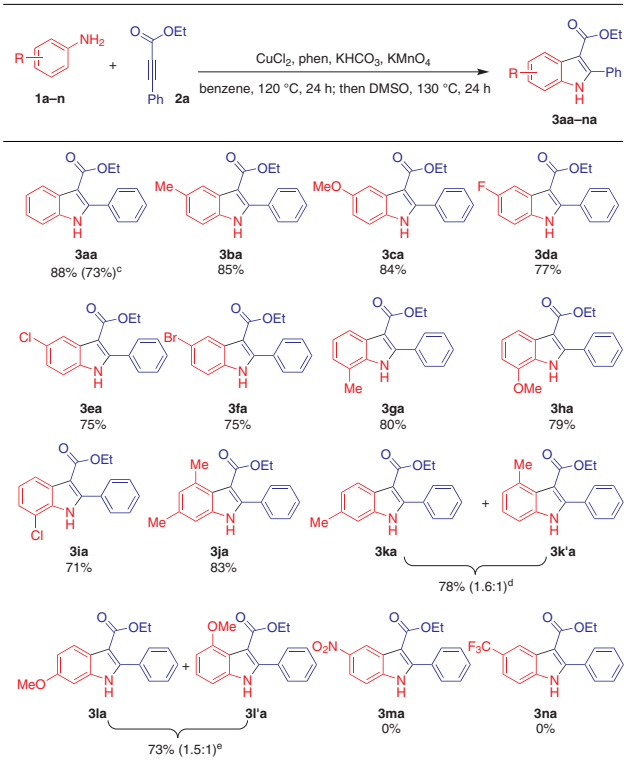
Entry	Copper salt	Ligand[b]	Base	Oxidant	Solvent	Yield (%)[c]
1	CuBr	**L1**	$KHCO_3$	O_2	MeCN; DMSO	8
2[d]	CuBr	**L1**	$KHCO_3$	O_2	MeCN; DMSO	NR
3	CuCl	**L1**	$KHCO_3$	O_2	MeCN; DMSO	12
4	$Cu(OTf)_2$	**L1**	$KHCO_3$	O_2	MeCN; DMSO	trace
5	$Cu(OAc)_2$	**L1**	$KHCO_3$	O_2	MeCN; DMSO	trace
6	$CuCl_2$	**L1**	$KHCO_3$	O_2	MeCN; DMSO	13
7	$CuCl_2$	**L2**	$KHCO_3$	O_2	MeCN; DMSO	NR
8	$CuCl_2$	**L3**	$KHCO_3$	O_2	MeCN; DMSO	NR
9	$CuCl_2$	**L4**	$KHCO_3$	O_2	MeCN; DMSO	7
10	$CuCl_2$	**L5**	$KHCO_3$	O_2	MeCN; DMSO	18
11	$CuCl_2$	**L6**	$KHCO_3$	O_2	MeCN; DMSO	25
12	$CuCl_2$	**L7**	$KHCO_3$	O_2	MeCN; DMSO	33
13	$CuCl_2$	**L7**	Li_2CO_3	O_2	MeCN; DMSO	NR
14	$CuCl_2$	**L7**	*t*-BuONa	O_2	MeCN; DMSO	28
15	$CuCl_2$	**L7**	NaOMe	O_2	MeCN; DMSO	19
16	$CuCl_2$	**L7**	NaOAc	O_2	MeCN; DMSO	13
17	$CuCl_2$	**L7**	NaOH	O_2	MeCN; DMSO	NR
18	$CuCl_2$	**L7**	Na_2CO_3	O_2	MeCN; DMSO	NR
19	$CuCl_2$	**L7**	Et_3N	O_2	MeCN; DMSO	NR
20	$CuCl_2$	**L7**	$KHCO_3$	$KMnO_4$	MeCN; DMSO	53
21	$CuCl_2$	**L7**	$KHCO_3$	1,4-BQ	MeCN; DMSO	NR
22	$CuCl_2$	**L7**	$KHCO_3$	$K_2S_2O_8$	MeCN; DMSO	32
23	$CuCl_2$	**L7**	$KHCO_3$	MnO_2	MeCN; DMSO	40
24	$CuCl_2$	**L7**	$KHCO_3$	$K_2Cr_2O_7$	MeCN; DMSO	38
25	$CuCl_2$	**L7**	$KHCO_3$	$KMnO_4$	THF; DMSO	18
26	$CuCl_2$	**L7**	$KHCO_3$	$KMnO_4$	DMF; DMSO	NR
27	$CuCl_2$	**L7**	$KHCO_3$	$KMnO_4$	toluene; DMSO	61
28	$CuCl_2$	**L7**	$KHCO_3$	$KMnO_4$	DCE; DMSO	NR
29	$CuCl_2$	**L7**	$KHCO_3$	$KMnO_4$	1,4-dioxane; DMSO	57
30	$CuCl_2$	**L7**	$KHCO_3$	$KMnO_4$	benzene; DMSO	88
31[e]	$CuCl_2$	**L7**	$KHCO_3$	$KMnO_4$	benzene; DMSO	trace (11[f]/32[g])

[a] Reaction conditions: **1a** (0.4 mmol), **2a** (0.2 mmol), copper salt (0.2 mmol), ligand (30 mol%), base (0.2 mmol), solvent (1 mL), O_2 (1 atm) or oxidant (0.2 mmol), 120 °C, 24 h; then DMSO (1 mL), 130 °C, 24 h.
[b] **L1**: 2-(Di-*tert*-butylphosphino)biphenyl; **L2**: 2-(Dicyclohexylphosphino)-2′-methylbiphenyl; **L3**: 2-Dicyclohexylphosphino-2,6-diisopropoxybiphenyl; **L4**: 1,3-Bis(2,4,6-trimethylphenyl)imidazolium chloride; **L5**: 2, 2-Bipyridine; **L6**: Glyoxime; **L7**: 1,10-Phenanthroline.
[c] Isolated yield after chromatography.
[d] A mixed solvent (MeCN/DMSO = 1:1) was directly used.
[e] $CuCl_2$: 15 mmol%.
[f] $CuCl_2$: 25 mmol%.
[g] $CuCl_2$: 50 mmol%.

and provided higher yields. However, the incorporation of strong electron-withdrawing group (NO_2 and CF_3) in the *para*-position of arylamine seriously hampered copper-mediated hydroamination of alkynes, and the corresponding indoles **3ma** and **3na** cannot be obtained. For *meta*-substituted arylamines **1k** and **1l**, regioselectivity issues

surfaced in the CDC process, and a mixture of two regioisomers was obtained. Intramolecular CDC reaction occurred at two different sites to give products **3ka**/**3k′a** (1.6:1) and **3la**/**3l′a** (1.5:1), respectively. In addition, disubstituted aromatic amine **1j** underwent the reaction smoothly and afforded the corresponding indole **3ja** in 83% yield. It is worth noting that when the reaction was carried out on a 1.0 mmol scale, the product **3aa** can be obtained in 73% yield.

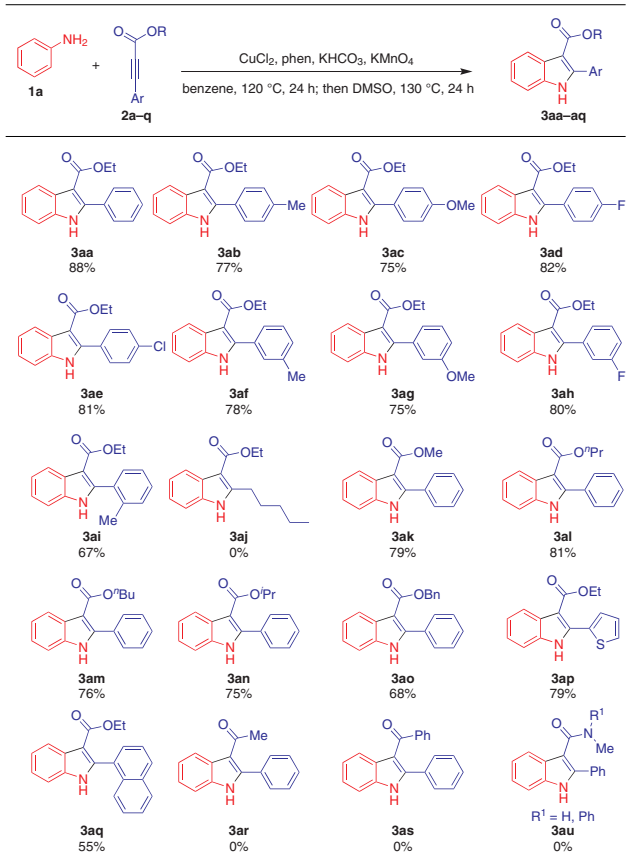
Table 2 Variation of Arylamine Substrates[a,b]



[a] Reaction conditions: **1** (0.4 mmol), **2a** (0.2 mmol), $CuCl_2$ (0.2 mmol), phen (30 mol%), $KHCO_3$ (0.2 mmol), benzene (1 mL), $KMnO_4$ (0.2 mmol), 120 °C, 24 h; then DMSO (1 mL), 130 °C, 24 h.
[b] Isolated yield after chromatography.
[c] One millimole scale.
[d] *m*-Toluidine was used, and the ratio of the regioisomers was determined by NMR analysis.
[e] 3-Methoxyaniline was used, and the ratio of the regioisomers was determined by NMR analysis.

The scope and generality of ester propiolates were next explored in this one-pot sequential process (Table 3). For ethyl arylpropiolates, the electronic nature of the aromatic motifs did not seem to affect the efficiency: both electron-donating (Me and MeO) and electron-withdrawing substituents (F and Cl) can be incorporated at the *ortho*- (**2i**), *meta*- (**2f**–**h**), and *para*-position (**2b**–**e**), providing indole derivatives **3ab**–**ai** in good to high yields (67–82%). In addition, heteroaryl (thiophene) and α-naphthylpropiolates **2p** and **2q** can also be efficiently transformed into the corresponding products **3ap** and **3aq** in 79% and 55% yield, respectively. However, when the scope of substrates was extended to aliphatic propiolate ester [ethyl oct-2-ynoate (**2j**)], ynones [4-phenylbut-3-yn-2-one (**2r**) and diphenylpropynone (**2s**)], and arylpropiolamides **2t** and **2u**, the reactions cannot proceed to provide the corresponding products **3aj** and **3ar**–**au**. Other alkyl arylpropiolates, such as methyl, *n*-propyl, *n*-butyl, isopropyl, and benzyl esters **2k**–**o** were also examined under the standard conditions, the reaction can smoothly proceed to give the corresponding products **3ak**–**ao** in high yields (68–81%).

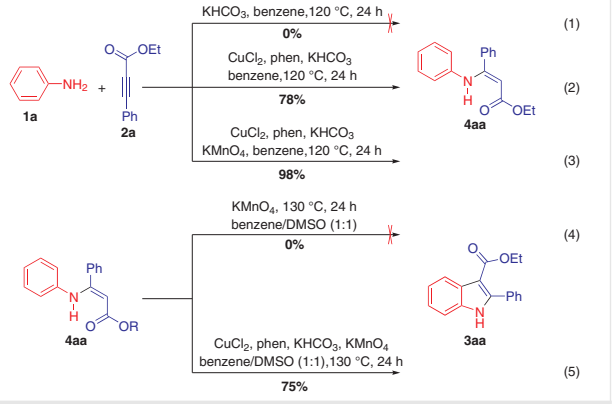
Table 3 Variation of Ester Arylpropiolates[a,b]



[a] Reaction conditions: **1a** (0.4 mmol), **2** (0.2 mmol), $CuCl_2$ (0.2 mmol), phen (30 mol%), $KHCO_3$ (0.2 mmol), benzene (1 mL), $KMnO_4$ (0.2 mmol), 120 °C, 24 h; then DMSO (1 mL), 130 °C, 24 h.
[b] Isolated yield after chromatography.

To gain insight into the mechanism of this sequential annulation process, some designed control experiments were conducted (Scheme 2). At first, the reaction of aniline (**1a**) and ethyl phenylpropiolate (**2a**) was examined in benzene at 120 °C for 24 hours in the presence of $KHCO_3$; however, the starting materials were completely recovered (Scheme 2, eq 1), which indicated that ethyl (*Z*)-3-phenyl-3-(phenylamino)acrylate (**4aa**) cannot be obtained through aza-Michael addition reaction.[12d] With $CuCl_2$ as the catalyst,

the reaction can give ethyl (*Z*)-3-phenyl-3-(phenylamino)-acrylate (**4aa**) specifically (Scheme 2, eq 2) even in the presence of stronger bases such as NaOH, NaOMe, and *t*-BuONa when using benzene as the sole solvent. Intermediate **4aa** was most probably derived from copper-mediated hydroamination of alkyne.[33] More interesting, the adduct **4aa** of **1a** and **2a** was isolated in higher yield (98%) in the presence of $KMnO_4$ as the oxidant (Scheme 2, eq 3); however, copper-mediated intramolecular CDC reaction of **4aa** cannot proceed further to give indole **3aa** only using benzene as the solvent. To demonstrate CDC process, **4aa** was isolated and tested in two different reaction conditions (Scheme 2, eqs 4 and 5). In the absence of $CuCl_2$/phen, $KMnO_4$ cannot promote this oxidative CDC reaction (Scheme 2, eq 4) in binary mixed solvents (benzene/DMSO, 1:1) at 130 °C. On the other hand, the target product **3aa** was obtained in 75% yield under the standard conditions (Scheme 2, eq 5), further confirming that the reaction pathway was comprised of intermolecular hydroamination of alkyne followed by an intramolecular copper-mediated oxidative CDC sequence.

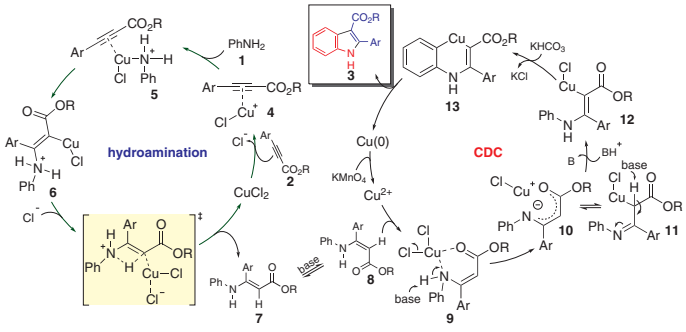


Scheme 2 Investigation of the reaction mechanism

On the basis of the above results, a plausible mechanism was outlined for this tandem reaction. Scheme 3 shows a simplified sequence of events beginning with the active Cu(II) species. The coordination of alkyne **2** to $CuCl_2$ promoted the dissociation of chloride anion from Cu(II) center, leading to the formation of cationic Cu(II)-alkyne complex **4**. Aniline **1** reacted with **4** possibly through two distinct pathways. The first pathway involved direct intermolecular nucleophilic attack of aniline **1** on the alkyne ligated to cationic copper center. However, this route was less likely since aromatic amines with electron-withdrawing groups should react faster. In fact, strong electron-withdrawing groups (NO_2 and CF_3) hampered copper-mediated hydroamination process. The other route, involving the coordination of aniline **1**, *syn* migratory insertion of alkyne into N–Cu, and protonation of C–Cu bond to give *E*-enamine **7**, appeared more probable. In the presence of base, **7** was then gradually isomerized into a more stable *Z*-isomer **8**. The coordination of *Z*-isomer **8** to Cu(II) gave a six-membered chelate ring complex **9**, which was then transformed into a new C–Cu(II) complex **11** through base-promoted deprotonation of NH, dissociation of chloride anion, and complexation of the resulting cationic Cu(II) species at α-carbon of **10**. Imine-containing Cu(II)-alkyl complex **11** was then transformed into alkenylcopper **12** through a deprotonation/re-protonation process under basic conditions. *Ortho*-metalation of aniline-tethered alkenyl Cu(II) complex **12** led to the formation of six-membered copper-cycle intermediate **13**, which was then transformed into indole **3**. Finally, Cu(0) resulting from reductive elimination process was oxidized to Cu(II) by $KMnO_4$.

In conclusion, we have developed a novel approach for the synthesis of C3-functionalized indoles, which are prominent structural motifs in many biologically active molecules. Using simple anilines as the starting materials, this tandem reaction sequence is comprised of copper-mediated intermolecular hydroamination of alkynes and intramolecular oxidative cross-dehydrogenative coupling in a one-pot manner.

Chemicals were purchased from commercial supplies and used without further purification, unless otherwise stated. Solvents were dried and purified according to the standard procedures before use. Reactions were monitored by analytical TLC. All reactions were conducted in dried glassware. Purification of reaction products was done by



Scheme 3 Proposed mechanism

flash chromatography with 230–400 mesh silica gel. Ester arylpropiolate substrates were prepared according to the literature methods.[34] Melting points were determined on a melting point apparatus in open capillaries and are uncorrected. ^{1}H NMR spectra were recorded on a 500 MHz spectrometer, and ^{13}C NMR spectra were recorded at 125 MHz. Unless otherwise stated, $CDCl_3$ was used as a solvent. Chemical shifts (δ) are given in parts per million downfield relative to TMS. Chemical shifts for carbon resonances are reported in parts per million and are referenced to the carbon resonance of the solvent $CHCl_3$ (δ = 77.16). Coupling constants are given in hertz (Hz). High-resolution mass spectra were recorded on a BIO TOF Q mass spectrometer equipped with an electrospray ion source (ESI), operated in the positive mode.

2-Arylindole-3-carboxylate Derivatives 3; General Procedure

A 10 mL Schlenk tube equipped with a magnetic stirring bar was charged with $CuCl_2$ (0.2 mmol, 26.9 mg), phenanthroline (0.07 mmol, 13 mg), $KHCO_3$ (20 mg, 0.2 mmol) and $KMnO_4$ (0.2 mmol, 31.6 mg), and then the respective arylamine **1** (0.4 mmol) and the appropriate ester arylpropiolate **2** (0.2 mmol) were added. Benzene (1.0 mL) was then added to the mixture via syringe at rt under air. The tube was sealed and kept in a preheated oil bath at 120 °C for 24 h. DMSO (1.0 mL) was finally added and the mixture was heated at 130 °C for a further 24 h. The mixture was cooled to rt, quenched with H_2O (5 mL), and diluted with CH_2Cl_2 (10 mL). The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic extracts were dried (anhyd Na_2SO_4), filtered, and concentrated in vacuo. The crude product was then purified by flash chromatography on silica gel (H), eluting with 10–20% EtOAc/PE.

Ethyl 2-Phenyl-1*H*-indole-3-carboxylate (3aa)

White solid; yield: 46.6 mg (88%); mp 157–159 °C (Lit.[35] mp 157–159 °C).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.79 (s, 1 H), 8.21 (d, *J* = 7.5 Hz, 1 H), 7.61–7.57 (m, 2 H), 7.39–7.34 (m, 3 H), 7.32–7.29 (m, 1 H), 7.28–7.20 (m, 2 H), 4.25 (q, *J* = 7.1 Hz, 2 H), 1.28 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 164.5, 143.6, 134.2, 131.0, 128.6, 128.0, 127.0, 126.6, 122.1, 121.0, 120.9, 110.1, 103.5, 58.7, 13.3.

Ethyl 5-Methyl-2-phenyl-1*H*-indole-3-carboxylate (3ba)

White solid; yield: 47.4 mg (85%); mp 137–139 °C (Lit.[35] mp 136–139 °C).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.77–8.66 (br, 1 H), 8.01 (s, 1 H), 7.57 (br, 2 H), 7.35 (br, 3 H), 7.19–7.17 (m, 1 H), 7.05 (d, *J* = 8.0 Hz, 1 H), 4.23 (q, *J* = 7.0 Hz, 2 H), 2.48 (s, 3 H), 1.25 (t, *J* = 7.0 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 165.7, 144.6, 133.6, 132.2, 131.4, 129.6, 129.0, 128.0, 127.9, 124.7, 121.7, 110.8, 104.1, 59.6, 21.8, 14.3.

Ethyl 5-Methoxy-2-phenyl-1*H*-indole-3-carboxylate (3ca)[36]

White solid; yield: 49.6 mg (84%); mp 148–150 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.78 (br, 1 H), 7.63 (d, *J* = 1.9 Hz, 1 H), 7.52–7.43 (m, 2 H), 7.27 (br, 3 H), 7.10 (d, *J* = 8.7 Hz, 1 H), 6.83–6.70 (m, 1 H), 4.14 (q, *J* = 7.1 Hz, 2 H), 3.77 (s, 3 H), 1.16 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 164.6, 154.7, 143.9, 131.2, 129.3, 129.2, 128.5, 127.9, 127.5, 126.9, 112.3, 111.0, 102.6, 58.6, 54.7, 13.2.

Ethyl 5-Fluoro-2-phenyl-1*H*-indole-3-carboxylate (3da)

Grayish white solid; yield: 43.6 mg (77%); mp 151–153 °C (Lit.[36] mp 152–154 °C).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.88 (s, 1 H), 7.75 (d, *J* = 8.8 Hz, 1 H), 7.47 (d, *J* = 4.9 Hz, 2 H), 7.25 (br, 3 H), 7.09 (dd, *J* = 8.6, 4.3 Hz, 1 H), 6.88–6.85 (m, 1 H), 4.13 (q, *J* = 7.0 Hz, 2 H), 1.19 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 165.4, 159.2 (d, $^1J_{C,F}$ = 235 Hz), 146.2, 131.7 (d, $^3J_{C,F}$ = 7 Hz), 129.5, 129.3, 128.3 (d, $^3J_{C,F}$ = 11 Hz), 128.1, 112.1, 112.0, 111.5 (d, $^2J_{C,F}$ = 26.5 Hz), 107.3 (d, $^2J_{C,F}$ = 25.3 Hz), 104.6 (d, $^4J_{C,F}$ = 4.3 Hz), 59.9, 14.3.

Ethyl 5-Chloro-2-phenyl-1*H*-indole-3-carboxylate (3ea)

Grayish white solid; yield: 44.9 mg (75%); mp 149–151 °C (Lit.[36] mp 151–153 °C).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.80 (s, 1 H), 8.17 (d, *J* = 1.3 Hz, 1 H), 7.59–7.57 (m, 2 H), 7.41–7.35 (m, 3 H), 7.23–7.17 (m, 2 H), 4.25 (q, *J* = 7.1 Hz, 2 H), 1.29 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 165.0, 145.7, 133.5, 131.5, 129.5, 129.4, 128.7, 128.1, 127.8, 123.5, 121.7, 112.1, 104.4, 59.9, 14.3.

Ethyl 5-Bromo-2-phenyl-1*H*-indole-3-carboxylate (3fa)

White solid; yield: 51.4 mg (75%); mp 102–104 °C (Lit.[35] mp 102–104 °C).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.73 (s, 1 H), 8.35 (s, 1 H), 7.60 (br, 2 H), 7.41 (br, 3 H), 7.33 (d, *J* = 8.4 Hz, 1 H), 7.20 (d, *J* = 8.3 Hz, 1 H), 4.27 (q, *J* = 7.0 Hz, 2 H), 1.29 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 165.0, 145.5, 133.8, 131.5, 129.6, 129.5, 129.3, 128.2, 126.2, 124.8, 115.6, 112.5, 104.4, 60.0, 14.3.

Ethyl 7-Methyl-2-phenyl-1*H*-indole-3-carboxylate (3ga)

White solid; yield: 44.6 mg (80%); mp 154–156 °C (Lit.[35] mp 155–157 °C).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.56 (s, 1 H), 8.06 (d, *J* = 8.0 Hz, 1 H), 7.68–7.55 (m, 2 H), 7.40–7.38 (m, 3 H), 7.18 (t, *J* = 7.6 Hz, 1 H), 7.05 (d, *J* = 7.1 Hz, 1 H), 4.26 (q, *J* = 7.1 Hz, 2 H), 2.48 (s, 3 H), 1.28 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 165.5, 144.3, 134.7, 132.2, 129.7, 129.0, 128.0, 127.2, 123.8, 122.2, 120.2, 119.8, 105.2, 59.6, 16.5, 14.3.

Ethyl 7-Methoxy-2-phenyl-1*H*-indole-3-carboxylate (3ha)[37]

White solid; yield: 46.6 mg (79%); mp 157–159 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.74 (s, 1 H), 7.80 (d, *J* = 8.1 Hz, 1 H), 7.72–7.57 (m, 2 H), 7.45–7.42 (m, 3 H), 7.18 (t, *J* = 8.0 Hz, 1 H), 6.71 (d, *J* = 7.8 Hz, 1 H), 4.30 (q, *J* = 7.1 Hz, 2 H), 3.94 (s, 3 H), 1.31 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 165.4, 145.8, 143.9, 132.1, 129.7, 129.1, 129.0, 128.1, 125.8, 122.5, 114.7, 105.3, 103.1, 59.7, 55.4, 14.4.

Ethyl 7-Chloro-2-phenyl-1*H*-indole-3-carboxylate (3ia)

White solid; yield: 42.5 mg (71%); mp 145–147 °C (Lit.[29m] mp 145–147 °C).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.66 (s, 1 H), 8.12 (d, *J* = 7.9 Hz, 1 H), 7.72–7.59 (m, 2 H), 7.51–7.37 (m, 3 H), 7.33–7.23 (m, 1 H), 7.20 (t, *J* = 7.8 Hz, 1 H), 4.30 (q, *J* = 7.1 Hz, 2 H), 1.30 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 164.8, 144.9, 132.5, 131.5, 129.7, 129.5, 129.0, 128.2, 122.8, 122.5, 120.9, 116.4, 105.9, 59.9, 14.3.

Ethyl 4,6-Dimethyl-2-phenyl-1*H*-indole-3-carboxylate (3ja)

White solid; yield: 48.7 mg (83%); mp 120–122 °C (Lit.[29n] mp 120–122 °C).

^{1}H NMR (500 MHz, $CDCl_3$); δ = 8.50 (s, 1 H), 7.56–7.39 (m, 2 H), 7.39–7.25 (m, 3 H), 6.88 (s, 1 H), 6.81 (s, 1 H), 4.17 (q, *J* = 7.1 Hz, 2 H), 2.61 (s, 3 H), 2.36 (s, 3 H), 1.11 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 167.1, 140.4, 136.1, 133.1, 132.5, 130.9, 128.7, 128.5, 128.2, 125.3, 123.6, 108.8, 106.9, 60.4, 21.4, 21.1, 13.9.

Mixture of Ethyl 6-Methyl-2-phenyl-1*H*-indole-3-carboxylate (3ka) and Ethyl 4-Methyl-2-phenyl-1*H*-indole-3-carboxylate (3k′a)[36,38]

Yellow oil; the ratio (**3ka**:**3k′a** = 1.6:1) was determined by ^{1}H NMR analysis; yield: 43.5 mg (78%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.92–8.61 (m, 2.4 $H_{overlap}$), 8.07 (d, *J* = 8.1 Hz, 1 $H_{3k'a}$), 7.58–7.56 (m, 1.6 H_{3ka}), 7.48–7.47 (m, 3.5 $H_{overlap}$), 7.34 (br, 8 $H_{overlap}$), 7.22–7.18 (m, 1.5 H_{3ka}), 7.17–7.06 (m, 6.3 $H_{overlap}$), 6.97 (d, *J* = 6.9 Hz, 2 $H_{3k'a}$), 4.27–4.20 (m, 2 $H_{3k'a}$), 4.21–4.16 (m, 3 H_{3ka}), 2.65 (s, 4.7 H_{3ka}), 2.42 (s, 3 $H_{3k'a}$), 1.26 (t, *J* = 7.0 Hz, 3 $H_{3k'a}$), 1.13 (t, *J* = 7.1 Hz, 4.9 H_{3ka}).

^{13}C NMR (151 MHz, $CDCl_3$): δ = 165.0, 164.9, 143.3, 137.7, 134.7, 133.6, 131.7, 131.1, 131.0, 130.6, 129.8, 128.5, 127.7, 127.6, 127.5, 127.4, 127.1, 126.7, 126.0, 124.6, 124.4, 124.3, 122.5, 122.1, 121.9, 120.4, 110.3, 108.2, 105.6, 102.8, 59.5, 58.6, 20.5, 20.1, 13.2, 12.8.

Mixture of Ethyl 6-Methoxy-2-phenyl-1*H*-indole-3-carboxylate (3la) and Ethyl 4-Methoxy-2-phenyl-1*H*-indole-3-carboxylate (3l′a)[36]

Yellow oil; the ratio (**3la**:**3l′a** = 1.5:1) was determined by ^{1}H NMR analysis; yield: 43.1 mg (73%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.12 (s, 0.9 H_{3la}), 8.97 (s, 0.8 $H_{3l'a}$), 8.05 (d, *J* = 8.8 Hz, 1 $H_{3l'a}$), 7.57–7.55 (m, 1.8 $H_{overlap}$), 7.50–7.47 (m, 2.2 $H_{overlap}$), 7.35–7.26 (m, 5.5 $H_{overlap}$), 7.09 (t, *J* = 8.0 Hz, 1 $H_{3l'a}$), 7.03 (t, *J* = 8.0 Hz, 1 $H_{3l'a}$), 6.92–6.84 (m, 1.8 $H_{overlap}$), 6.73 (d, *J* = 1.8 Hz, 1 $H_{3l'a}$), 6.54 (d, *J* = 7.9 Hz, 1 $H_{3l'a}$), 6.31 (dd, *J* = 8.2, 2.1 Hz, 1 $H_{3l'a}$), 6.26 (dd, *J* = 7.9, 1.6 Hz, 1 $H_{3l'a}$), 6.21 (t, *J* = 2.2 Hz, 1 $H_{3l'a}$), 4.42–4.02 (m, 4.5 $H_{overlap}$), 3.83 (s, 3 $H_{3l'a}$), 3.71 (s, 4.6 H_{3la}), 1.27 (t, *J* = 7.1 Hz, 4.3 H_{3la}), 1.19 (t, *J* = 7.1 Hz, 3 $H_{3l'a}$).

^{13}C NMR (151 MHz, $CDCl_3$): δ = 166.4, 164.7, 155.7, 152.4, 142.8, 137.8, 136.0, 135.2, 131.0, 130.7, 128.4, 127.6, 127.3, 127.3, 127.2, 126.8, 122.8, 121.5, 120.7, 115.8, 110.7, 104.8, 103.5, 102.9, 100.6, 93.5, 59.7, 58.6, 54.4, 54.3, 13.2, 13.0.

Ethyl 2-(*p*-Tolyl)-1*H*-indole-3-carboxylate (3ab)

White solid; yield: 42.9 mg (77%); mp 145–147 °C (Lit.[29n] mp 144–146 °C).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.64 (s, 1 H), 8.20 (d, *J* = 7.2 Hz, 1 H), 7.51 (d, *J* = 8.0 Hz, 2 H), 7.35–7.31 (m, 1 H), 7.26–7.23 (m, 2 H), 7.19 (d, *J* = 7.9 Hz, 2 H), 4.29 (q, *J* = 7.1 Hz, 2 H), 2.36 (s, 3 H), 1.32 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 165.5, 144.9, 139.3, 135.1, 129.5, 129.0, 128.8, 127.7, 123.0, 122.1, 122.0, 111.0, 104.4, 59.7, 21.4, 14.4.

Ethyl 2-(4-Methoxyphenyl)-1*H*-indole-3-carboxylate (3ac)

White solid; yield: 44.2 mg (75%); mp 164–165 °C (Lit.[36] mp 165–167 °C).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.82 (s, 1 H), 8.18 (d, *J* = 7.7 Hz, 1 H), 7.52 (d, *J* = 8.7 Hz, 2 H), 7.29–7.19 (m, 3 H), 6.84 (d, *J* = 8.7 Hz, 2 H), 4.27 (q, *J* = 7.1 Hz, 2 H), 3.75 (s, 3 H), 1.32 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 165.7, 160.2, 144.8, 135.1, 130.9, 127.6, 124.1, 122.9, 122.0, 121.9, 113.5, 111.1, 103.9, 59.7, 55.3, 14.4.

Ethyl 2-(4-Fluorophenyl)-1*H*-indole-3-carboxylate (3ad)

White solid; yield: 46.4 mg (82%); mp 166–168 °C (Lit.[35] mp 166–168 °C).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.73 (s, 1 H), 8.20 (dd, *J* = 6.2, 2.3 Hz, 1 H), 7.62–7.56 (m, 2 H), 7.35 (dd, *J* = 6.0, 2.2 Hz, 1 H), 7.28–7.25 (m, 2 H), 7.08 (t, *J* = 8.6 Hz, 2 H), 4.29 (q, *J* = 7.1 Hz, 2 H), 1.32 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 164.4, 162.2 (d, $^1J_{C,F}$ = 249.4 Hz), 142.5, 134.1, 130.5 (d, $^3J_{C,F}$ = 8.4 Hz), 127.0, 126.9, 126.4, 122.3, 121.1 (d, $^4J_{C,F}$ = 3.5 Hz), 114.1 (d, $^2J_{C,F}$ = 21.8 Hz), 110.0, 103.7, 58.8, 13.3.

Ethyl 2-(4-Chlorophenyl)-1*H*-indole-3-carboxylate (3ae)

White solid; yield: 48.1 mg (81%); mp 151–153 °C (Lit.[35] mp 152–155 °C).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.68 (s, 1 H), 8.23–8.16 (m, 1 H), 7.56 (d, *J* = 8.4 Hz, 2 H), 7.39–7.33 (m, 3 H), 7.31–7.23 (m, 2 H), 4.30 (q, *J* = 7.1 Hz, 2 H), 1.33 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 165.3, 143.1, 135.3, 135.2, 130.9, 130.4, 128.3, 127.4, 123.5, 122.2, 122.2, 111.1, 105.0, 59.9, 14.3.

Ethyl 2-(*m*-Tolyl)-1*H*-indole-3-carboxylate (3af)

White solid; yield: 43.5 mg (78%); mp 143–145 °C (Lit.[29m] mp 144–146 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.58 (s, 1 H), 8.14 (d, *J* = 7.5 Hz, 1 H), 7.35–7.33 (d, *J* = 6.5 Hz, 2 H), 7.24 (t, *J* = 6.3 Hz, 1 H), 7.22–7.14 (m, 3 H), 7.12 (d, *J* = 7.7 Hz, 1 H), 4.19 (q, *J* = 7.1 Hz, 2 H), 2.28 (s, 3 H), 1.22 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 164.5, 143.7, 136.6, 134.1, 130.9, 129.1, 128.8, 126.9, 126.6, 125.8, 122.0, 121.0, 120.9, 110.0, 103.4, 58.6, 20.3, 13.3.

Ethyl 2-(3-Methoxyphenyl)-1*H*-indole-3-carboxylate (3ag)

White solid; yield: 44.3 mg (75%); mp 136–138 °C (Lit.[29n] mp 136–138 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.81 (s, 1 H), 8.23–8.16 (m, 1 H), 7.35–7.21 (m, 4 H), 7.20–7.11 (m, 2 H), 6.90 (d, *J* = 8.2 Hz, 1 H), 4.27 (q, *J* = 7.1 Hz, 2 H), 3.77 (s, 3 H), 1.30 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 165.5, 159.1, 144.3, 135.1, 133.2, 129.1, 127.6, 123.1, 122.0, 121.9, 115.3, 114.6, 111.2, 111.1, 104.5, 59.7, 55.3, 14.3.

Ethyl 2-(3-Fluorophenyl)-1*H*-indole-3-carboxylate (3ah)

White solid; yield: 45.2 mg (80%); mp 160–162 °C (Lit.[29m] mp 162–164 °C).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.72 (s, 1 H), 8.25–8.17 (m, 1 H), 7.41–7.34 (m, 4 H), 7.31–7.22 (m, 2 H), 7.14–7.02 (m, 1 H), 4.30 (q, *J* = 7.1 Hz, 2 H), 1.32 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 165.3, 162.3 (d, $^1J_{C,F}$ = 246 Hz), 142.7, 135.2, 134.0 (d, $^3J_{C,F}$ = 8 Hz), 129.7 (d, $^3J_{C,F}$ = 8 Hz), 129.2, 127.5, 125.3 (d, $^4J_{C,F}$ = 3 Hz), 123.5, 122.3, 116.9 (d, $^2J_{C,F}$ = 23 Hz), 116.1 (d, $^2J_{C,F}$ = 21 Hz), 111.1, 105.2, 59.9, 14.3.

Ethyl 2-(*o*-Tolyl)-1*H*-indole-3-carboxylate (3ai)

White solid; yield: 37.4 mg (67%); mp 76–79 °C (Lit.[35] mp 76–79 °C).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.74 (s, 1 H), 8.23–8.04 (m, 1 H), 7.59–7.45 (m, 1 H), 7.35–7.29 (m, 2 H), 7.19–7.17 (m, 2 H), 7.05–6.84 (m, 2 H), 4.20 (q, *J* = 7.1 Hz, 2 H), 3.74 (s, 3 H), 1.20 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 164.3, 155.9, 140.0, 134.0, 131.7, 129.6, 126.1, 121.9, 120.9, 120.6, 119.5, 119.3, 110.0, 109.9, 104.6, 58.5, 54.6, 13.3.

Methyl 2-Phenyl-1*H*-indole-3-carboxylate (3ak)

White solid; yield: 39.7 mg (79%); mp 135–137 °C (Lit.[29n] mp 135–137 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.72 (s, 1 H), 8.24–8.13 (m, 1 H), 7.63–7.60 (m, 2 H), 7.44–7.39 (m, 3 H), 7.34 (dd, *J* = 6.1, 2.3 Hz, 1 H), 7.30–7.21 (m, 2 H), 3.80 (s, 3 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 165.9, 144.7, 135.2, 131.9, 129.6, 129.2, 128.8, 128.2, 127.5, 123.2, 122.1, 111.2, 104.4, 50.9.

Propyl 2-Phenyl-1*H*-indole-3-carboxylate (3al)

White solid; yield: 45.2 mg (81%); mp 116–118 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.87 (s, 1 H), 8.12 (d, *J* = 7.8 Hz, 1 H), 7.47–7.45 (m, 2 H), 7.24–7.23 (m, 3 H), 7.20–7.08 (m, 3 H), 4.03 (t, *J* = 6.6 Hz, 2 H), 1.59–1.52 (m, 2 H), 0.79 (t, *J* = 7.4 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 164.7, 143.7, 134.2, 131.0, 128.6, 128.0, 126.9, 126.6, 122.0, 120.9, 110.2, 103.4, 64.5, 21.0, 9.6.

ESI-MS: *m*/*z* = 279 [M^+], 280 [M + 1]$^+$.

HRMS-ESI: *m*/*z* [M + H]$^+$ calcd for $C_{18}H_{18}NO_2$: 280.1338; found: 280.1334.

Butyl 2-Phenyl-1*H*-indole-3-carboxylate (3am)[38]

White solid; yield: 44.5 mg (76%); mp 154–156 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.55 (s, 1 H), 8.22–8.06 (m, 1 H), 7.55–7.53 (m, 2 H), 7.36–7.30 (m, 3 H), 7.30–7.24 (m, 1 H), 7.23–7.12 (m, 2 H), 4.14 (t, *J* = 6.6 Hz, 2 H), 1.58–1.53 (m, 2 H), 1.29–1.21 (m, 2 H), 0.82 (t, *J* = 7.4 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 164.5, 143.5, 134.1, 131.1, 128.6, 128.1, 127.0, 126.6, 122.1, 121.1, 121.0, 110.0, 103.7, 62.6, 29.8, 18.3, 12.7.

Isopropyl 2-Phenyl-1*H*-indole-3-carboxylate (3an)[39]

White solid; yield: 41.9 mg (75%); mp 124–126 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.73 (s, 1 H), 8.14 (d, *J* = 7.6 Hz, 1 H), 7.57–7.41 (m, 2 H), 7.33–7.25 (m, 3 H), 7.23 (d, *J* = 7.5 Hz, 1 H), 7.18–7.12 (m, 2 H), 5.08 (hept, *J* = 6.2 Hz, 1 H), 1.18 (d, *J* = 6.2 Hz, 6 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 164.0, 143.5, 134.2, 131.1, 128.6, 128.0, 126.9, 126.6, 122.0, 121.0, 120.9, 110.1, 103.9, 66.0, 21.0.

Benzyl 2-Phenyl-1*H*-indole-3-carboxylate (3ao)[29m]

White solid; yield: 44.5 mg (68%); mp 164–165 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.68 (s, 1 H), 8.17–8.06 (m, 1 H), 7.46 (d, *J* = 6.5 Hz, 2 H), 7.29–7.16 (m, 9 H), 7.15–7.13 (m, 2 H), 5.17 (s, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 164.1, 143.9, 135.4, 134.1, 130.9, 128.6, 128.1, 127.4, 127.1, 127.0, 126.8, 126.6, 122.1, 121.1, 121.0, 110.1, 103.2, 64.5.

Ethyl 2-(Thiophen-2-yl)-1*H*-indole-3-carboxylate (3ap)[23f]

White solid; yield: 42.8 mg (79%); mp 155–157 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.02 (br, 1 H), 8.09–8.07 (m, 1 H), 7.52 (d, *J* = 3.5 Hz, 1 H), 7.26 (d, *J* = 5.0 Hz, 1 H), 7.21 (d, *J* = 8.0 Hz, 1 H), 7.16–7.10 (m, 2 H), 6.91 (t, *J* = 4.2 Hz, 1 H), 4.27 (q, *J* = 7.1 Hz, 2 H), 1.30 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 164.6, 136.4, 134.2, 131.4, 128.3, 126.8, 126.5, 126.1, 122.4, 121.1, 121.0, 110.0, 103.6, 59.0, 13.4.

Ethyl 2-(Naphthalen-1-yl)-1*H*-indole-3-carboxylate (3aq)[35]

White solid; yield: 34.6 mg (55%); mp 166–168 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.57 (br, 1 H), 8.23 (d, *J* = 7.8 Hz, 1 H), 7.86 (d, *J* = 8.0 Hz, 1 H), 7.81 (d, *J* = 8.1 Hz, 1 H), 7.60 (d, *J* = 8.5 Hz, 1 H), 7.48–7.39 (m, 3 H), 7.33–7.28 (m, 2 H), 7.27–7.19 (m, 2 H), 3.92 (d, *J* = 7.1 Hz, 2 H), 0.75 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 163.9, 141.5, 134.2, 132.2, 131.2, 129.5, 128.4, 127.2, 126.9, 126.2, 125.5, 125.1, 124.7, 123.8, 122.2, 121.1, 120.9, 110.0, 106.2, 58.3, 12.7.

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Supporting Information

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