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Hydrogen-Transfer-Mediated *N*-Arylation of Naphthols Using Indolines as Hydrogen Donors

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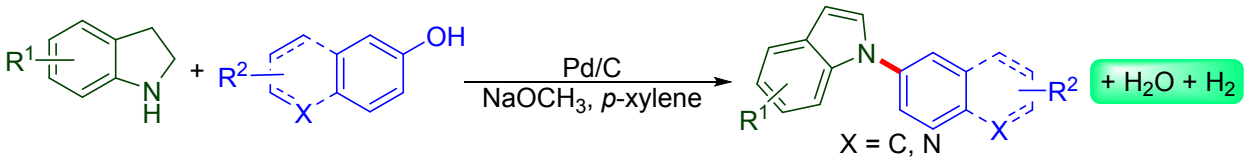


- Hydrogen transfer reaction
- Indolines as reagents and hydrogen donors
- C-N bond formation
- H_2O and H_2 as by-product

ABSTRACT: Using a hydrogen-transfer-mediated activation mode, we report a new catalytic system for the transfer hydrogenation of naphthols. In the presence of Pd/C catalyst and base, various naphthols reacted with indolines to afford *N*-aryl-substituted heterocyclic compounds. Indolines were found to act as a novel hydrogen donors for naphthols under palladium catalysis. This method features good functional tolerance, operational simplicity, and a readily available catalyst.

INTRODUCTION

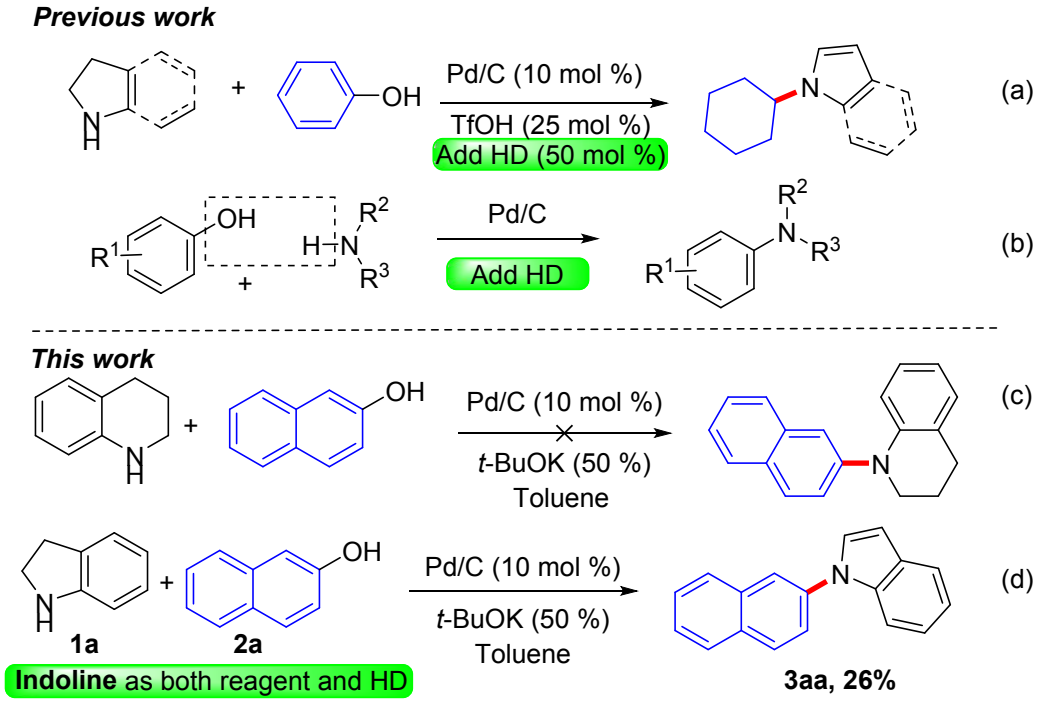
N-Arylheterocycles are important building blocks in medicinal, biological, and organic chemistry.[1] N-Arylindoles are of interest as antipsychotic agents,[2] melatonin receptor agonists, partial agonists,[3] antipsychotic agents,[4] and synthetic intermediates in the preparation of other biologically active heterocyclic agents.[5] Indoles and naphthalenes are common substructures in natural products. The synthesis of these simple structures, or their introduction into complex molecules, would not only have significant potential biological applications, but also represent a significant contribution to synthetic methodology.[6] In the last decades, much effort has been directed

toward improving C–N bond formation reactions to synthesis of N-arylated heterocycles.[7] Traditionally, Pd and Cu catalysts have been used for C–N bond formations. However, current aryl halide-based strategies require the pre-synthesis of aryl halides and generate unwanted halide waste.[8] Therefore, researchers should aim to develop more efficient and environmentally friendly cross-coupling methods to construct N-arylindoles.

Hydrogen transfer-mediated C–N bond formations have emerged as powerful tools in synthetic organic chemistry.[7b, 9] The direct coupling of phenols, instead of haloarenes, has long been a synthetic aspiration and significant scientific challenge. Li's group developed a highly efficient Pd/C-catalyzed formal direct cross-coupling of phenols with various amines and anilines using sodium formate as hydrogen donor (HD) under transfer hydrogenation conditions.[10] More recently, Li and coworkers described a palladium-catalyzed formal aromaticity transfer coupling reaction between phenols and pyrrolidines or indolines to generate the corresponding N-cyclohexyl pyrroles or indoles using $NaBH_4$ as hydrogen donor (Scheme 1a).[11] Recently, Li's group have reported a palladium-catalyzed formal direct cross-coupling of phenols with various amines and anilines through a tandem reduction/condensation/dehydrogenation process (Scheme 1b).[12] As part of our continuing research interest in the construction of functional N-heterocycles through hydrogen transfer,[13] we have recently reported an iridium-catalyzed hydrogen-transfer-mediated α-functionalization of 1,8-naphthyridines using tetrahydroquinolines (THQs) as inactive hydrogen donors [14]. These previous studies prompted us to explore the transfer hydrogenation cross-coupling of THQ with 2-naphthols, in which THQ serves as both reagent and hydrogen donor (Scheme 1c). THQs does not react in this system because THQ is difficult to dehydrogenate relative to indoline in

this catalytic system, so it cannot transfer hydrogenation process. Interestingly, we observed that, using indoline instead of THQ under Pd/C catalysis and *t*-BuOK conditions, 2-naphthol was successfully *N*-arylated to give desired product **3aa** in 26% (Scheme 1d). Compared with conventional HDs (such as alcohols,[15] NH_3BH_3,[16] Hantzsch esters,[17] HCO_2H,[18] and $NaCO_2H$[10]), indolines derivatives, which are readily available, and easy to handle, were novel hydrogen donors in hydrogen transfer reactions, providing a new and promising approach to future transfer hydrogenations.

Scheme 1. Unexpected new transfer hydrogenation system

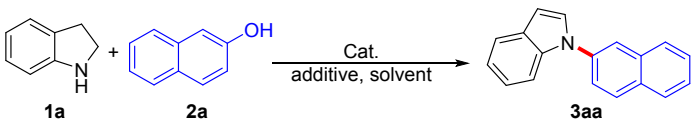


RESULTS AND DISCUSSION

Our initial studies focused on developing a more efficient catalyst system for the coupling of indoline **1a** and 2-naphthol **2a** as a model reaction. First, conventional bases were tested by performing the reaction in toluene at 130 °C for 12 h under N_2 protection. Many bases were tested, including *t*-BuOK, *t*-BuONa, HCO_2Na, NaOH, and $NaOCH_3$ (Table 1, entries 1–5). The results

showed that $NaOCH_3$ was the most effective base, affording product **3aa** in 49% yield. However, using CF_3CO_2H or no base failed to afford any desired product (entries 6 and 7). A control experiment without catalyst afforded no product, confirming that the catalyst was essential to the reaction (Table 1, entry 8). When various palladium catalysts were tested, Pd/C gave the best results (Table 1, entries 9–11). Next, several solvents were examined in combination with $NaOCH_3$ (entries 12–15), with *p*-xylene giving the best result (59% yield, entry 13). The best yield of **3aa** (68%) was obtained when the reaction was conducted in *p*-xylene at 130 °C for 24 h. Finally, by changing the reaction temperature to 140 °C, the yield was increased to 76% yield (entry 17). When we reduce the content of Pd/C catalyst, we find that the yield of Pd/C catalyst (10 wt%, 10 mol% based on Pd content) is greatly reduced. Therefore, the conditions shown in entry 17 (Table 1) were selected as optimal conditions.

Table 1. Screening of optimal reaction conditions[a]



1a 2a 3aa

Entry	**Cat.** (10 mol %)	Additive (50 mol %)	Solvent	**3aa** (yield %)[b]
1	Pd/C	*t*-BuOK	Toluene	31
2	Pd/C	*t*-BuONa	Toluene	34
3	Pd/C	HCO_2Na	Toluene	44
4	Pd/C	NaOH	Toluene	22
5	Pd/C	$NaOCH_3$	Toluene	49
6	Pd/C	TFA	Toluene	Trace
7	Pd/C	-	Toluene	Trace
8	-	$NaOCH_3$	Toluene	-
9	$PdCl_2$	$NaOCH_3$	Toluene	-
10	$Pd(PPh_3)_4$	$NaOCH_3$	Toluene	-
11	$Pd(dba)_2$	$NaOCH_3$	Toluene	14

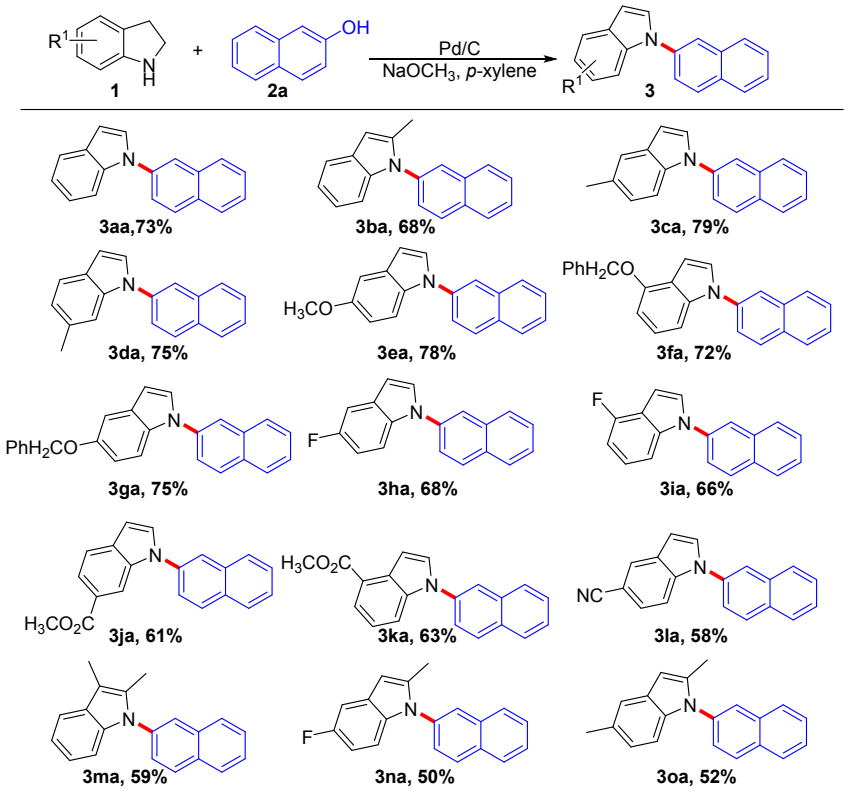
12	Pd/C	$NaOCH_3$	Dioxane	40
13	Pd/C	$NaOCH_3$	*p*-xylene	59
14	Pd/C	$NaOCH_3$	DMSO	Trace
15	Pd/C	$NaOCH_3$	DMF	Trace
16	Pd/C	$NaOCH_3$	*p*-xylene	68[c]
17	Pd/C	$NaOCH_3$	*p*-xylene	(76, 74, 71)[d]
18	Pd/C	$NaOCH_3$	*p*-xylene	(62, 41)[e]

[a]Reaction conditions: Unless otherwise stated, all reactions were performed with **1a** (42.8 mg, 0.36 mmol), **2a** (43.2 mg, 0.3 mmol), catalyst (31.8mg, 10 mol%), and base (8.1mg, 50 mol%) in solvent (1.5 mL) at 130 °C by oil-bath heating for 16 h under N_2 protection. [b]Isolated yield. [c]After reacting for 24 h. [d]Yields obtained at temperatures at 140, 150, and 160 °C, respectively. [e] Pd/C (6 mol%, 2 mol %).

With optimized conditions in hand, the indoline substrate scope was explored. As shown in Scheme 2, different indolines reacted efficiently with 2-naphthol **2a**, furnishing desired products **3aa**–**3oa** in moderate to good isolated yields. Various indolines bearing electron-withdrawing and electron-donating groups all reacted smoothly. Furthermore, substituent positioning at the *meta*- or *para*-positions of the benzene ring only slightly affected the product yields (Scheme 2, **3ca** and **3da**). Obvious electronic effects were observed in the reactions of substituted indolines, with electron-donating groups resulting in relatively high yields (**3ca**–**3ga**) and electron-withdrawing groups (**3ha-3la**) resulting in relatively low yields. This phenomenon was attributed to the electron-donating substituents enhancing the nucleophilicity of the corresponding indoles, which favored the trapping of cyclohexenone intermediates (Scheme 2). Similarly, disubstituted indolines (**1m**–**1o**) underwent effective coupling to give desired products **3ma**–**3oa**. We tested some pyrrolidines and found that no target products were obtained. It may be that pyrrolidines are more difficult to dehydrogenate relative to indoline in this catalytic system. According to the literature,[19] we have tried to test the coupling reaction of indoles and naphthol under this conditions using

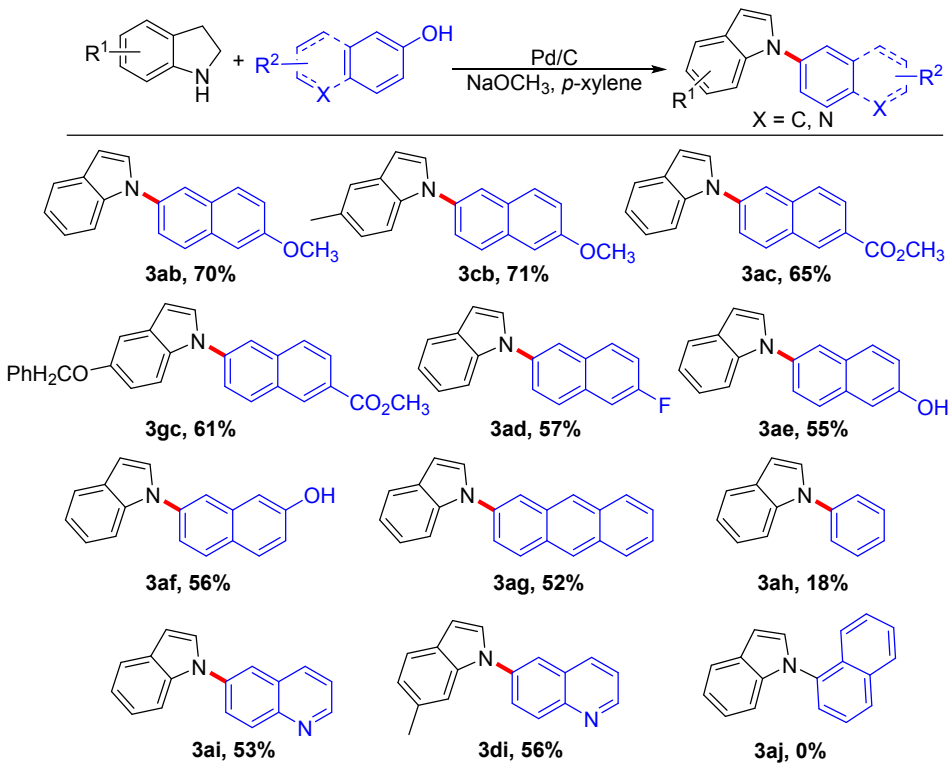
HCO_2H/HCO_2K as hydrogen source, but failed to give product, probably because the N atom on the indole is weakly nucleophilic.

Scheme 2. Substrate scope of indolines [a]



[a] Standard conditions: **1a** (0.36 mmol), 2 (0.3 mmol), Pd/C (10 mol %), and base (50 mol %) in *p*-xylene (1.5 mL) at 140 °C for 24 h.

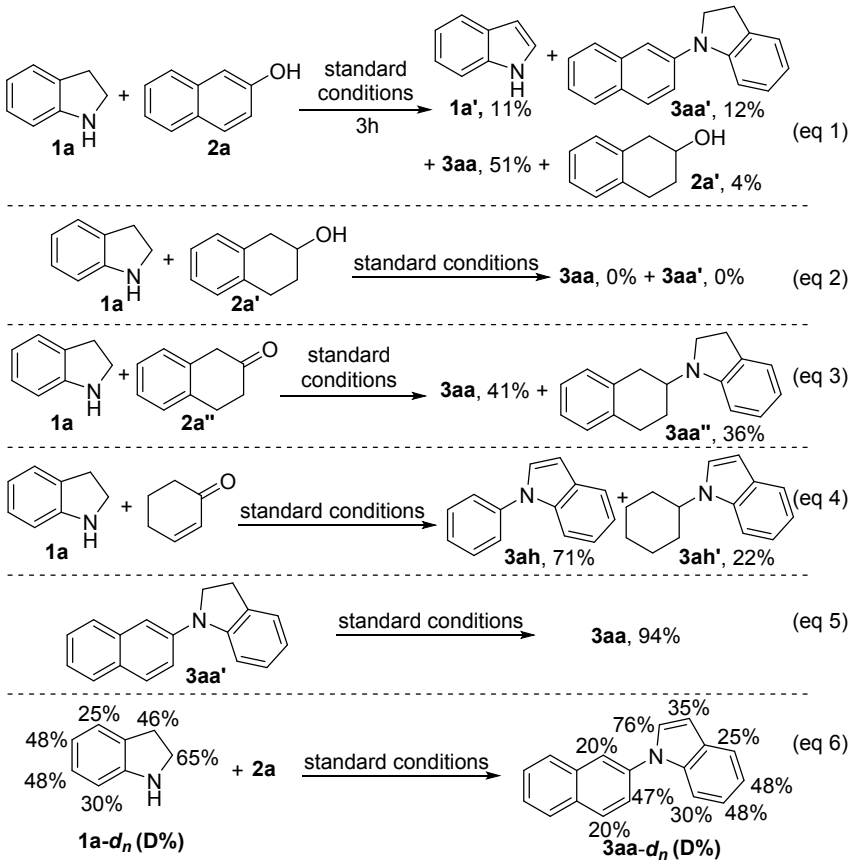
Scheme 3. Variation of both coupling partners



Next, we focused on varying both coupling partners (Scheme 3). Reactions of indolines **1** with various naphthols **2** were explored. Similar to the results described in Scheme 3, all reactions proceeded efficiently to afford the desired products in moderate to good isolated yields (**3ab**–**3di**). Various naphthols bearing electron-withdrawing or electron-donating groups were all suitable substrates in this transformation, with the corresponding products obtained in moderate to good yields. Furthermore, naphthols bearing electron-donating substituents provided the desired products in higher yields than those bearing electron-withdrawing substituents (**3ab**–**3gc**). When 2,6-naphthalenediol and 2,7-dihydroxynaphthalene were used as starting materials, only one C–N bond was formed (**3ae**, **3af**). Interestingly, 2-hydroxyanthracene reacted smoothly with indoline to afford desired *N*-arylation product **3ag**. However, the reaction of phenol **2h** with indoline **1a** afforded only a low yield (**3ah**, 18%), it is possible that phenol is more difficult to hydrogenate than naphthol in this catalytic system using indoline as hydrogen donor. Interestingly, the catalytic system was also

compatible with the transformation of 6-hydroxyquinoline, affording the new indole-quinoline linked biheteroarenes (**3ai**, **3di**). When using 1-naphthol as a substrate, unfortunately no target product (**3aj**) was obtained.

Scheme 4. Control experiments

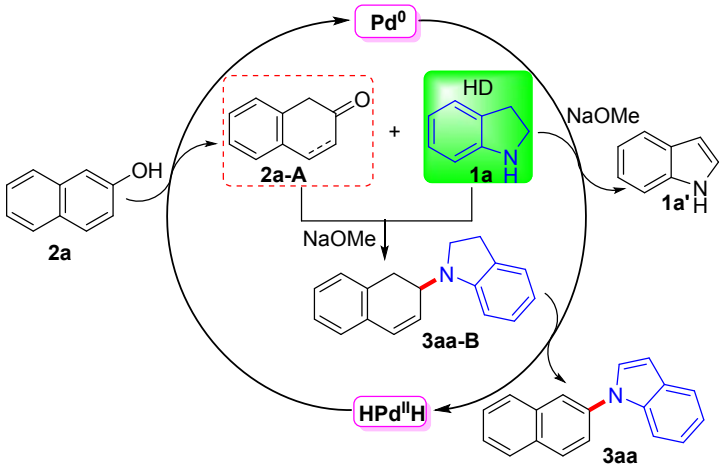


To gain insight into the reaction mechanism, several control experiments were performed (Scheme 4). The model reaction was interrupted after 3 h to analyze the intermediates. Product **3aa**, indole **1a'**, **3aa'**, and 1,2,3,4-tetrahydro-2-naphthalenol **2a'** were detected in 51%, 11%, 12%, and 4% yields, respectively (Scheme 4, Eq. 1). The reaction of **2a'** with indoline **1a** under the standard conditions failed to give product **3aa** (Eq. 2), supporting that suppressing the formation of over-hydrogenated tetrahydronaphthalenol **2a'** was the key factor in chemoselective generation of product **3aa**. The reaction of **1a** reacting with β-tetralone gave products **3aa** and **3aa''** in 41% and

36% yields, respectively (Eq. 3). When we tried to separate **3aa''**, we found that **3aa''** rapidly converts to the other intermediate. Further control experiments suggested that both cyclohexanone and cyclohexenone might be reaction intermediates (Eq. 4). Furthermore, reacting **3aa'** under the standard reaction conditions gave product **3aa** in 94% yield (Eq. 5), indicating that **3aa'** was a key reaction intermediate. The deuterium-labelling experiment of indoline 1a-d_n with **2a** resulted in product 3aa-d_n, with incorporation of deuterium on the naphthalene unit, suggesting that hydrogen was transferred from indoline **1a** to 2-naphthol **2a** (Eq. 6). The naphthol **2a** is initially activated by hydrogen transfer of [DPd(II)D] arising from the metal catalyst, affording cyclohexen-1-ol intermediate and its tautomer cyclohexen-2-ol (in this tautomeric process, the D ratio was different on the naphthol ring).

Based on the above results, a tentative mechanism for this hydrogen transfer reaction was proposed, as shown in Scheme 5. Initially, the Pd-catalyzed dehydrogenation of indoline **1a** (1.5 eq.) forms an active $HPd^{II}H$ species, which performs the first hydrogenation of the 2-naphthol ring to form activated intermediate **2a**-A and regenerated the active palladium catalyst. Under NaOMe conditions, intermediate **2a**-A undergoes fast condensation with indoline **1a** to give key intermediate **3aa-B**. The role of NaOMe is to promote the conversion of naphthol to cyclohexenone intermediate under this condition. Next, desired product **3aa** can be obtained by palladium-catalyzed dehydrogenation of intermediate **3aa-B** to regenerate the $HPd^{II}H$ species.

Scheme 5. Plausible reaction pathways



CONCLUSIONS

In summary, a hydrogen-transfer-mediated activation mode for non-activated naphthols has been developed to achieve the simple, efficient, and novel N-arylation of naphthols using indolines as both reagent and hydrogen donor. The developed chemistry features operational simplicity, a readily available catalyst, good functional tolerance, and a wide substrate scope. This method offers a significant basis for the further development of new protocols for directly transforming or functionalizing inert *N*-arylated indoles. In addition, the reaction employed indoline as the hydrogen donor, avoiding the use of a potentially hazardous pressurized H_2 atmosphere. Indoline is a novel hydrogen donor in hydrogen transfer reactions, providing a promising new approach to future transfer hydrogenations.

EXPERIMENTAL SECTION

General Information. All experiments were carried out under the standard conditions. Flash column chromatography was performed over silica gel (200−300 mesh). All the obtained products were characterized by melting points (m.p), ^{1}H NMR and ^{13}C $\{^{1}H\}$ NMR spectra were recorded on a Bruker-AV (400 and 100 MHz, respectively) instrument internally referenced to TMS, chloroform and DMSO signals. MS analyses were performed on an Agilent 5975 GC−MS instrument (EI). High resolution mass spectra (HRMS) were recorded using electrospray ionization (ESI) and

time-of-flight (TOF) mass analysis. Melting points were uncorrected. The new compounds were characterized by ^{1}H NMR, ^{13}C {^{1}H} NMR, MS and HRMS. Unless otherwise stated, all the reagents were purchased from commercial sources (J&KChemic, TCI, Fluka, Acros, SCRC), used without further purification.

Typical procedure for the synthesis of 3. In a 25 mL Schlenk tube was combined Indolines **1** (0.36 mmol), Naphthols **2** (0.30 mmol), Pd/C (10 wt%, 10 mol% based on Pd content) and $NaOCH_3$ (50 mol%) in *P*-xylene (1.5 mL). The mixture was then stirred at 140 °C under oil-bath heating for 24 h. After cooling down to room temperature, the reaction mixture was concentrated by removing the solvent under vacuum, and the residue was purified by preparative TLC on silica, eluting with petroleum ether (60-90 °C): ethyl acetate (50:1) to give **3**.

Synthesis of *1-(naphthalen-2-yl)-1H-indole (3aa)*: Under N_2 atmosphere, Indoline **1a** (0.4 g, 3.6 mmol), 2-Naphthol **2a** (0.4 g, 3 mmol), Pd/C (318 mg, 10 wt%, 10 mol% based on Pd content) and $NaOCH_3$ (81 mg, 50 mol%) in *P*-xylene (5.0 mL) were introduced into a Schlenk tube (50 mL), successively. Then, the Schlenk tube was closed and the resulting mixture was stirred at 140 °C for 24 h. Purification of the residue by column chromatography (50:1 petroleum ether: ethyl acetate) gave **3aa** as a yellow solid (0.5 g, 68% yield). Yellow solid; m.p: 90.9-92.7 °C; R_f = 0.3 (petroleum ether/ethyl acetate = 50/1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 8.7 Hz, 1H), 8.01 – 7.88 (m, 3H), 7.80 (d, *J* = 6.7 Hz, 1H), 7.76 – 7.67 (m, 2H), 7.66 – 7.54 (m, 2H), 7.50 (d, *J* = 3.1 Hz, 1H), 7.39 – 7.26 (m, 2H), 6.81 (d, *J* = 3.2 Hz, 1H). ^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 137.4, 136.2, 133.9, 131.9, 129.7, 129.5, 128.23, 127.9, 127.8, 127.0, 126.1, 123.3, 122.6, 122.0, 121.3, 120.6, 110.7, 103.9. HRMS (ESI) m/z calcd for $C_{18}H_{14}N$ $[M+H]^+$: 244.1121; found 244.1113.

2-methyl-1-(naphthalen-2-yl)-1H-indole (3ba). Yellow oil (54.7 mg, 56% yield); R_f = 0.3 (petroleum ether/ethyl acetate = 50/1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 8.6 Hz, 1H), 7.98 (dd, *J* = 6.0, 3.5 Hz, 1H), 7.91 (dd, *J* = 6.0, 3.5 Hz, 1H), 7.87 (d, *J* = 1.7 Hz, 1H), 7.67 – 7.62 (m, 1H), 7.60 (dd, *J* = 6.2, 3.3 Hz, 2H), 7.48 (dd, *J* = 8.6, 2.0 Hz, 1H), 7.21 – 7.10 (m, 3H), 6.49 (s, 1H), 2.38 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 138.4, 137.3, 135.5, 133.7, 132.6, 129.4, 128.4, 128.0, 127.9, 126.8, 126.6, 126.4, 126.2, 121.2, 120.2, 119.7, 110.1, 101.5, 13.5. HRMS (ESI) m/z calcd for $C_{19}H_{16}N$ $[M+H]^+$: 258.1277; found 258.1271.

5-methyl-1-(naphthalen-2-yl)-1H-indole (3ca). Yellow solid (59.4 mg, 77% yield); m.p: 164.9-167.3 °C; R_f = 0.3 (petroleum ether/ethyl acetate = 50/1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 8.7 Hz, 1H), 7.88 – 7.77 (m, 3H), 7.60 (dd, *J* = 8.7, 1.9 Hz, 1H), 7.57 – 7.43 (m, 4H), 7.35 (d, *J* = 3.1 Hz, 1H), 7.04 (d, *J* = 8.3 Hz, 1H), 6.62 (d, *J* = 2.3 Hz, 1H), 2.46 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 137.6, 134.5, 134.0, 133.9, 131.8, 129.9, 129.6, 128.2, 127.9, 127.8, 126.9, 126.0, 124.2, 123.2, 121.6, 120.9, 110.4, 103.5, 21.5. HRMS (ESI) m/z calcd for $C_{19}H_{16}N$ $[M+H]^+$: 258.1277; found 258.1271.

6-methyl-1-(naphthalen-2-yl)-1H-indole (3da). Yellow oil (57.8 mg, 75% yield); R_f = 0.3 (petroleum ether/ethyl acetate = 50/1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 8.7 Hz, 1H), 7.99 – 7.89 (m, 3H), 7.68 (dd, *J* = 15.9, 8.3 Hz, 2H), 7.62 – 7.53 (m, 2H), 7.49 (s, 1H), 7.41 (d, *J* = 3.1 Hz, 1H), 7.09 (d, *J* = 8.0 Hz, 1H), 6.73 (s, 1H), 2.52 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 137.5, 136.6, 133.9, 132.4, 131.9, 129.6, 127.9, 127.8, 127.7, 127.3, 126.9, 126.1, 123.5, 122.3, 122.0, 120.9, 110.5, 103.7, 22.0. HRMS (ESI) m/z calcd for $C_{19}H_{16}N$ $[M+H]^+$: 258.1277; found 258.1271.

5-methoxy-1-(naphthalen-2-yl)-1H-indole (3ea). Yellow oil (63.9mg, 78% yield); R_f = 0.3 (petroleum ether/ethyl acetate = 50/1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, *J* = 8.7 Hz, 1H), 7.96 – 7.86 (m, 3H), 7.67 (dd, *J* = 8.7, 2.1 Hz, 1H), 7.62 – 7.52 (m, 3H), 7.45 (d, *J* = 3.1 Hz, 1H), 7.23 (s, 1H), 6.97 (d, *J* = 8.9 Hz, 1H), 6.70 (d, *J* = 3.0 Hz, 1H), 3.93 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 154.8, 137.5, 133.9, 131.8, 131.4, 130.1, 129.6, 128.6, 127.9, 127.7, 127.0, 126.0, 123.1, 121.5, 112.6, 111.5, 103.6, 102.9, 55.9. HRMS (ESI) m/z calcd for $C_{19}H_{16}NO$ $[M+H]^+$: 274.1226; found 274.1219.

4-(benzyloxy)-1-(naphthalen-2-yl)-1H-indole (3fa). Yellow oil (73.3 mg, 70% yield); R_f = 0.3 (petroleum ether/ethyl acetate = 50/1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 – 7.68 (m, 4H), 7.50 (d, *J* = 8.7 Hz, 1H), 7.46 – 7.35 (m, 4H), 7.28 (t, *J* = 7.4 Hz, 2H), 7.21 (d, *J* = 2.7 Hz, 2H), 7.14 (d, *J* = 8.2 Hz, 1H), 7.02 (dd, *J* = 15.6, 7.6 Hz, 1H), 6.80 (s, 1H), 6.54 (d, *J* = 7.7 Hz, 1H), 5.13 (s, 2H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 152.8, 137.7, 137.5, 133.9, 131.9, 129.6, 128.6, 127.9, 127.9, 127.8, 127.4, 127.0, 126.8, 126.2, 123.4, 123.4, 122.0, 120.5, 104.4, 102.0, 101.5, 70.1. HRMS (ESI) m/z calcd for $C_{25}H_{20}NO$ $[M+H]^+$: 350.1539; found 350.1531.

5-(benzyloxy)-1-(naphthalen-2-yl)-1H-indole (3ga). Red solid (78.5 mg, 75% yield); m.p: 115.2-117.3 °C; R_f = 0.3 (petroleum ether/ethyl acetate = 50/1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, *J* = 8.7 Hz, 1H), 7.98 – 7.86 (m, 3H), 7.68 (dd, *J* = 8.7, 2.1 Hz, 1H), 7.65 – 7.54 (m, 5H), 7.51 – 7.43 (m, 3H), 7.40 (t, *J* = 7.2 Hz, 1H), 7.33 (d, *J* = 2.0 Hz, 1H), 7.08 (dd, *J* = 8.9, 2.1 Hz, 1H), 6.72 (d, *J* = 3.1 Hz, 1H), 5.21 (s, 2H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 153.9, 137.8, 137.5, 134.0, 131.8, 131.6, 130.1, 129.7, 128.7, 128.6, 127.9, 127.9, 127.8, 127.6, 127.0, 126.1, 123.1, 121.5, 113.4, 111.5, 104.6, 103.7, 70.9. HRMS (ESI) m/z calcd for $C_{25}H_{20}NO$ $[M+H]^+$: 350.1539; found 350.1528.

5-fluoro-1-(naphthalen-2-yl)-1H-indole (3ha). Yellow oil (46.9 mg, 60% yield); R_f = 0.3 (petroleum ether/ethyl acetate = 50/1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 8.7 Hz, 1H), 7.82 (dd, *J* = 15.9, 8.5 Hz, 3H), 7.61 – 7.42 (m, 4H), 7.34 (dd, *J* = 3.1, 1.3 Hz, 1H), 7.28 (d, *J* = 7.6 Hz, 1H), 6.94 (dd, *J* = 8.4, 7.0 Hz, 1H), 6.65 (d, *J* = 2.6 Hz, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 160.4 (d, *J* = 237.9 Hz), 137.0, 136.2 (d, *J* = 12.0 Hz), 133.9, 132.0, 129.9, 128.7 (d, *J* = 3.5 Hz), 127.9, 127.8, 127.1, 126.3, 125.9, 122.9, 122.0, 121.9, 109.3 (d, *J* = 24.5 Hz), 103.9, 97.2 (d, *J* = 27.1 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -119.8. HRMS (ESI) m/z calcd for $C_{18}H_{13}FN$ $[M+H]^+$: 262.1027; found 262.1021.

4-fluoro-1-(naphthalen-2-yl)-1H-indole (3ia). Yellow oil (47.7 mg, 61% yield); R_f = 0.3 (petroleum ether/ethyl acetate = 50/1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.7 Hz, 1H), 7.99 – 7.86 (m, 3H), 7.65 (dd, *J* = 8.7, 2.1 Hz, 1H), 7.63 – 7.53 (m, 2H), 7.50 – 7.37 (m, 2H), 7.18 (dd, *J* = 13.4, 7.8 Hz, 1H), 6.91 (t, *J* = 7.9 Hz, 1H), 6.86 (s, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 156.5 (d, *J* = 247.4 Hz), 138.7 (d, *J* = 11.0 Hz), 137.0, 133.8, 132.1, 129.7, 128.2, 127.9, 127.8, 127.1, 126.4, 123.2, 123.0 (d, *J* = 7.7 Hz), 122.3, 118.5 (d, *J* = 23.0 Hz), 106.8 (d, *J* = 3.4 Hz), 105.3 (d, *J* = 18.9 Hz), 99.8. ^{19}F NMR (376 MHz, $CDCl_3$) δ -121.7. HRMS (ESI) m/z calcd for $C_{18}H_{13}FN$ $[M+H]^+$: 262.1027; found 262.1038.

Methyl 1-(naphthalen-2-yl)-1H-indole-6-carboxylate (3ja). Yellow solid (46.1 mg, 51% yield); m.p: 150-151 °C; R_f = 0.3 (petroleum ether/ethyl acetate = 50/1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (s, 1H), 8.05 (d, *J* = 8.7 Hz, 1H), 7.99 – 7.87 (m, 4H), 7.77 (d, *J* = 8.3 Hz, 1H), 7.68 (d, *J* = 8.6 Hz, 1H), 7.64 – 7.54 (m, 3H), 6.80 (d, *J* = 3.1 Hz, 1H), 3.94 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)

δ 168.0, 136.6, 135.7, 133.8, 132.9, 132.2, 131.4, 129.9, 127.9, 127.9, 127.1, 126.4, 124.3, 123.3, 122.5, 121.6, 120.8, 112.9, 103.9, 51.9. HRMS (ESI) m/z calcd for $C_{20}H_{16}NO_2$ $[M+H]^+$: 302.1176; found 302.1171.

Methyl 1-(naphthalen-2-yl)-1H-indole-4-carboxylate (3ka). Yellow oil (47.9 mg, 53% yield); R_f = 0.3 (petroleum ether/ethyl acetate = 50/1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 – 7.98 (m, 2H), 7.97 – 7.88 (m, 3H), 7.82 (d, *J* = 8.2 Hz, 1H), 7.65 – 7.54 (m, 4H), 7.45 (d, *J* = 3.0 Hz, 1H), 7.31 (t, *J* = 8.0 Hz, 1H), 4.07 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 167.9, 137.0, 136.8, 133.8, 132.1, 130.3, 129.8, 128.9, 127.9, 127.8, 127.1, 126.4, 124.0, 123.4, 122.6, 122.1, 121.7, 115.4, 104.9, 51.9. HRMS (ESI) m/z calcd for $C_{20}H_{16}NO_2$ $[M+H]^+$: 302.1176; found 302.1188.

1-(naphthalen-2-yl)-1H-indole-5-carbonitrile (3la). Yellow solid (43.4 mg, 54% yield); m.p: 133.6-137.5 °C; R_f = 0.3 (petroleum ether/ethyl acetate = 50/1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 – 7.96 (m, 2H), 7.94 – 7.89 (m, 1H), 7.86 (d, *J* = 5.7 Hz, 2H), 7.60 – 7.52 (m, 4H), 7.50 (d, *J* = 3.3 Hz, 1H), 7.41 (dd, *J* = 8.6, 1.2 Hz, 1H), 6.76 (d, *J* = 3.3 Hz, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 137.7, 136.1, 133.7, 132.3, 130.6, 130.0, 129.1, 128.0, 127.9, 127.4, 126.7, 126.7, 125.4, 123.0, 122.7, 120.6, 111.5, 104.4, 103.6. HRMS (ESI) m/z calcd for $C_{19}H_{13}N_2$ $[M+H]^+$: 269.1073; found 269.1066.

2,3-dimethyl-1-(naphthalen-2-yl)-1H-indole (3ma). Yellow solid (48.0 mg, 59% yield); m.p: 87-89.1°C; R_f = 0.3 (petroleum ether/ethyl acetate = 50/1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 – 7.98 (m, 2H), 7.94 (dd, *J* = 6.0, 3.4 Hz, 1H), 7.89 (s, 1H), 7.71 – 7.59 (m, 3H), 7.51 (dd, *J* = 8.6, 1.5 Hz, 1H), 7.28 – 7.10 (m, 3H), 2.44 (s, 3H), 2.36 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 137.6, 135.9, 133.8, 133.1, 132.4, 132.4, 129.3, 129.0, 127.9, 127.9, 126.8, 126.5, 126.3, 121.3, 119.7, 118.0, 109.8, 108.3, 11.1, 8.9. HRMS (ESI) m/z calcd for $C_{20}H_{18}N$ $[M+H]^+$: 272.1434; found 272.1426.

5-fluoro-2-methyl-1-(naphthalen-2-yl)-1H-indole (3na). Yellow oil (36.3 mg, 44% yield); R_f = 0.3 (petroleum ether/ethyl acetate = 50/1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, *J* = 8.6 Hz, 1H), 7.93 – 7.88 (m, 1H), 7.86 – 7.81 (m, 1H), 7.77 (d, *J* = 1.6 Hz, 1H), 7.60 – 7.49 (m, 2H), 7.37 (dd, *J* = 8.6, 2.0 Hz, 1H), 7.22 (dd, *J* = 9.5, 2.4 Hz, 1H), 6.98 (dd, *J* = 8.9, 4.4 Hz, 1H), 6.79 (td, *J* = 9.1, 2.5 Hz, 1H), 6.38 (s, 1H), 2.30 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 158.4 (d, *J* = 234.3 Hz), 139.1,

135.3, 135.1, 133.7, 132.6, 129.6, 128.7 (d, *J* = 10.2 Hz), 127.9 (d, *J* = 4.2 Hz), 126.9, 126.8, 126.4, 125.9, 110.7 (d, *J* = 9.6 Hz), 109.3, 109.1, 104.6 (d, *J* = 23.6 Hz), 101.6 (d, *J* = 4.2 Hz), 13.59 . ^{19}F NMR (376 MHz, $CDCl_3$) δ -124.6. HRMS (ESI) m/z calcd for $C_{19}H_{15}NF$ $[M+H]^+$: 276.1183; found 276.1188.

2,5-dimethyl-1-(naphthalen-2-yl)-1H-indole (3oa). Yellow solid (40.6 mg, 50% yield); m.p: 99.7-100.3 °C; R_f = 0.3 (petroleum ether/ethyl acetate = 50/1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 8.6 Hz, 1H), 7.92 (dd, *J* = 6.0, 3.4 Hz, 1H), 7.85 (dd, *J* = 6.1, 3.3 Hz, 1H), 7.80 (d, *J* = 1.3 Hz, 1H), 7.59 – 7.51 (m, 2H), 7.42 (dd, *J* = 8.6, 2.0 Hz, 1H), 7.37 (s, 1H), 7.02 (d, *J* = 8.3 Hz, 1H), 6.90 (d, *J* = 8.2 Hz, 1H), 6.35 (s, 1H), 2.44 (s, 3H), 2.31 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 137.3, 136.8, 135.7, 133.7, 132.5, 129.4, 129.3, 128.6, 127.9, 127.9, 126.8, 126.5, 126.3, 126.1, 122.7, 119.5, 109.8, 101.2, 21.5, 13.5. HRMS (ESI) m/z calcd for $C_{20}H_{18}N$ $[M+H]^+$: 272.1434; found 272.1426.

1-(6-methoxynaphthalen-2-yl)-1H-indole (3ab). White oil (55.7 mg, 68% yield); R_f = 0.3 (petroleum ether/ethyl acetate = 50/1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 – 7.90 (m, 2H), 7.83 (d, *J* = 8.9 Hz, 2H), 7.75 – 7.64 (m, 2H), 7.49 (d, *J* = 2.7 Hz, 1H), 7.39 – 7.26 (m, 4H), 6.82 (d, *J* = 0.7 Hz, 1H), 4.02 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 158.0, 136.3, 135.5, 133.2, 129.4, 129.3, 129.2, 128.3, 128.3, 123.9, 122.4, 122.2, 121.3, 120.4, 119.9, 110.6, 105.9, 103.6, 55.4. HRMS (ESI) m/z calcd for $C_{19}H_{16}NO$ $[M+H]^+$: 274.1226; found 274.1219.

1-(6-methoxynaphthalen-2-yl)-5-methyl-1H-indole (3cb). Yellow oil (60.3 mg, 70% yield); R_f = 0.3 (petroleum ether/ethyl acetate = 50/1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 – 7.68 (m, 2H), 7.63 (d, *J* = 8.9 Hz, 1H), 7.47 (d, *J* = 8.6 Hz, 1H), 7.38 (s, 2H), 7.25 (d, *J* = 2.9 Hz, 1H), 7.15 – 7.03 (m, 2H), 6.94 (d, *J* = 8.5 Hz, 1H), 6.52 (s, 1H), 3.82 (s, 3H), 2.37 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 157.9, 135.7, 134.6, 133.0, 129.7, 129.7, 129.3, 129.2, 128.3, 128.2, 123.9, 123.8, 121.9, 120.8, 119.8, 110.3, 105.9, 103.1, 55.4, 21.4. HRMS (ESI) m/z calcd for $C_{20}H_{18}NO$ $[M+H]^+$: 288.1383; found 288.1376.

*Methyl 6-(1H-indol-1-yl)-2-naphthoate (3ac)***.** Yellow solid (41.6 mg, 46% yield); m.p: 75-77.8 °C; R_f = 0.3 (petroleum ether/ethyl acetate = 50/1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.66 (s, 1H), 8.15 – 8.06 (m, 2H), 7.95 (d, *J* = 1.2 Hz, 1H), 7.90 (d, *J* = 8.6 Hz, 1H), 7.75 – 7.70 (m, 2H), 7.67 (d,

J = 8.1 Hz, 1H), 7.44 (d, *J* = 3.3 Hz, 1H), 7.30 – 7.17 (m, 2H), 6.75 (d, J = 3.2 Hz, 1H), 4.00 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 167.1, 139.4, 136.1, 135.8, 131.1, 130.9, 130.7, 129.7, 127.9, 127.8, 127.5, 126.4, 123.8, 122.8, 121.4, 121.2, 120.8, 110.6, 104.6, 52.3. HRMS (ESI) m/z calcd for $C_{20}H_{16}NO_2$ $[M+H]^+$: 302.1176; found 302.1172.

Methyl 6-(5-methoxy-1H-indol-1-yl)-2-naphthoate (3gc). White oil (54.9 mg, 45% yield); R_f = 0.3 (petroleum ether/ethyl acetate = 50/1, v/v); ^1H NMR (400 MHz, $CDCl_3$) δ 8.69 (s, 1H), 8.16 (dd, *J* = 8.6, 1.4 Hz, 1H), 8.10 (d, *J* = 8.8 Hz, 1H), 7.99 – 7.90 (m, 2H), 7.74 (dd, J = 8.7, 2.1 Hz, 1H), 7.62 (d, *J* = 9.0 Hz, 1H), 7.53 (d, *J* = 7.4 Hz, 2H), 7.44 (dd, *J* = 11.9, 5.3 Hz, 3H), 7.37 (d, *J* = 7.3 Hz, 1H), 7.28 (d, *J* = 2.7 Hz, 1H), 7.04 (dd, *J* = 8.9, 2.3 Hz, 1H), 6.69 (d, *J* = 3.2 Hz, 1H), 5.18 (s, 2H), 4.04 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 167.1, 154.1, 139.5, 137.6, 136.2, 131.2, 131.1, 130.9, 130.6, 130.3, 128.6, 128.3, 127.9, 127.8, 127.5, 127.4, 126.4, 123.5, 120.7, 113.5, 111.4, 104.7, 104.4, 70.8, 52.3. HRMS (ESI) m/z calcd for $C_{27}H_{22}NO_3$ $[M+H]^+$: 408.1594; found 408.1599.

1-(6-fluoronaphthalen-2-yl)-1H-indole (3ad). Yellow oil(42.3 mg, 54% yield); R_f = 0.3 (petroleum ether/ethyl acetate = 20/1, v/v); ^1H NMR (500 MHz, $CDCl_3$) δ 7.96 (dd, *J* = 5.3, 3.3 Hz, 2H), 7.90 (dd, *J* = 9.0, 5.5 Hz, 1H), 7.78 (d, J = 8.1 Hz, 1H), 7.73 (dd, *J* = 8.8, 1.8 Hz, 1H), 7.67 (d, *J* = 7.5 Hz, 1H), 7.58 (dd, *J* = 9.6, 2.5 Hz, 1H), 7.47 (d, *J* = 3.2 Hz, 1H), 7.43 – 7.36 (m, 1H), 7.35 – 7.23 (m, 2H), 6.79 (dd, J = 3.2, 0.6 Hz, 1H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 160.8 (d, *J* = 246.5 Hz), 136.8 (d, *J* = 2.7 Hz), 136.0, 132.5 (d, *J* = 9.2 Hz), 130.8, 130.1 (d, *J* = 8.8 Hz), 129.4, 128.9 (d, *J* = 5.4 Hz), 128.1, 124.4, 122.6, 122.0, 121.3, 120.6, 117.5 (d, *J* = 25.6 Hz), 111.1 (d, *J* = 20.9 Hz), 110.5, 103.9. ^{19}F NMR (471 MHz, $CDCl_3$) δ -114.2. HRMS (ESI) m/z calcd for $C_{18}H_{13}FN$ $[M+H]^+$: 262.1027; found 262.1021.

6-(1H-indol-1-yl)naphthalen-2-ol (3ae). Yellow oil (38.8 mg, 50% yield); R_f = 0.3 (petroleum ether/ethyl acetate = 50/1, v/v); ^1H NMR (400 MHz, $CDCl_3$) δ 7.72 (s, 1H), 7.68 – 7.59 (m, 3H), 7.47 (t, *J* = 8.1 Hz, 2H), 7.29 (d, *J* = 2.9 Hz, 1H), 7.17 – 6.99 (m, 4H), 6.61 (d, *J* = 2.9 Hz, 1H), 5.49 (s, 1H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 153.8, 136.3, 135.4, 133.2, 129.7, 129.3, 129.1, 128.3, 127.9, 124.1, 122.4, 122.3, 121.2, 120.4, 118.9, 110.6, 109.7, 103.5. HRMS (ESI) m/z calcd for $C_{18}H_{14}NO$ $[M+H]^+$: 260.1070; found 260.1064.

*7-(1H-indol-1-yl)naphthalen-2-ol (3af)***.** Yellow solid (31.9 mg, 41% yield); m.p: 90-91.4°C; R_f = 0.3 (petroleum ether/ethyl acetate = 50/1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, *J* = 8.7 Hz, 1H), 7.83 (d, *J* = 9.4 Hz, 1H), 7.77 (d, *J* = 7.8 Hz, 2H), 7.69 (d, *J* = 7.9 Hz, 1H), 7.53 (dd, *J* = 8.6, 2.0 Hz, 1H), 7.46 (d, *J* = 3.2 Hz, 1H), 7.33 – 7.22 (m, 2H), 7.20 – 7.14 (m, 2H), 6.77 (d, *J* = 2.9 Hz, 1H), 5.75 (s, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 154.5, 138.0, 136.1, 135.2, 129.8, 129.5, 129.4, 128.2, 127.3, 122.5, 121.25, 120.9, 120.5, 120.4, 118.1, 110.7, 109.4, 103.8. HRMS (ESI) m/z calcd for $C_{18}H_{14}NO$ $[M+H]^+$: 260.1070; found 260.1064.

1-(anthracen-2-yl)-1H-indole (3ag). Yellow solid (29.9 mg, 34% yield); m.p: 186.6-189.9 °C; R_f = 0.3 (petroleum ether/ethyl acetate = 50/1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 (d, *J* = 18.3 Hz, 2H), 8.11 (d, *J* = 9.0 Hz, 1H), 8.06 – 7.93 (m, 3H), 7.71 (dd, *J* = 13.4, 7.9 Hz, 2H), 7.64 (dd, *J* = 9.0, 1.9 Hz, 1H), 7.53 – 7.42 (m, 3H), 7.29 – 7.16 (m, 2H), 6.74 (d, J = 3.2 Hz, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 136.7, 136.1, 132.4, 131.8, 131.8, 131.7, 130.1, 130.1, 129.5, 128.3, 128.1, 128.0, 126.5, 126.1, 126.0, 125.6, 123.4, 122.6, 121.3, 120.6, 110.8, 104.0. HRMS (ESI) m/z calcd for $C_{22}H_{16}N$ $[M+H]^+$: 294.1277; found 294.1270.

1-phenyl-1H-indole (3ah). Yellow oil (10.4 mg, 18% yield); R_f = 0.3 (petroleum ether/ethyl acetate = 50/1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.7 Hz, 1H), 7.62 (d, *J* = 8.2 Hz, 1H), 7.56 (d, *J* = 4.2 Hz, 4H), 7.44 – 7.38 (m, 2H), 7.31 – 7.19 (m, 2H), 6.74 (d, *J* = 3.2 Hz, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 139.9, 135.9, 129.6, 129.4, 127.9, 126.5, 124.4, 122.4, 121.2, 120.4, 110.5, 103.6. HRMS (ESI) m/z calcd for $C_{14}H_{12}N$ $[M+H]^+$: 194.0964; found 194.0981.

6-(1H-indol-1-yl)quinolone (3ai). Yellow oil (38.8 mg, 53% yield); R_f = 0.3 (petroleum ether/ethyl acetate = 10/1, v/v); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.97 (d, *J* = 4.1 Hz, 1H), 8.29 (d, *J* = 8.9 Hz, 1H), 8.17 (d, *J* = 8.1 Hz, 1H), 7.94 – 7.86 (m, 2H), 7.77 (d, *J* = 7.7 Hz, 1H), 7.68 (d, *J* = 8.1 Hz, 1H), 7.50 – 7.43 (m, 2H), 7.33 – 7.23 (m, 2H), 6.79 (d, *J* = 3.2 Hz, 1H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 150.5, 146.6, 137.8, 135.9, 135.8, 131.2, 129.6, 128.8, 127.9, 126.6, 122.8, 122.0, 121.4, 121.2, 120.8, 110.5, 104.5. HRMS (ESI) m/z calcd for $C_{17}H_{13}N_2$ $[M+H]^+$: 245.1073; found 245.1088.

6-(6-methyl-1H-indol-1-yl)quinoline (3di). Yellow oil (43.3 mg, 53% yield); R_f = 0.3 (petroleum ether/ethyl acetate = 10/1, v/v); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.98 (d, *J* = 3.0 Hz, 1H), 8.31 (d, *J* =

8.9 Hz, 1H), 8.25 (d, *J* = 8.3 Hz, 1H), 7.95 (dd, *J* = 8.9, 2.2 Hz, 1H), 7.92 (s, 1H), 7.63 (d, *J* = 8.0 Hz, 1H), 7.52 (dd, *J* = 8.2, 4.1 Hz, 1H), 7.47 (d, *J* = 0.6 Hz, 1H), 7.40 (d, *J* = 3.3 Hz, 1H), 7.08 (dd, *J* = 8.0, 0.9 Hz, 1H), 6.73 (dd, *J* = 3.3, 0.7 Hz, 1H), 2.50 (s, 3H). $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) δ 150.2, 146.3, 138.1, 136.3, 136.1, 132.7, 130.9, 128.9, 127.4, 127.3, 126.9, 122.6, 121.9, 121.3, 120.9, 110.3, 104.3, 21.9. HRMS (ESI) m/z calcd for $C_{18}H_{15}N_2$ $[M+H]^+$: 259.1230; found 259.1213.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.XXX.

^{1}H and ^{13}NMR spectra for the products (PDF)

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Notes

The authors declare no competing financial interest.

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