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PAPER

Pd(II)-Catalyzed Ligand Controlled Synthesis of Methyl 1-benzyl-1*H*-indole-3-carboxylates and Bis(1-benzyl-1*H*-indol-3-yl)methanones

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A simple change of ligand and solvent allows controlled, effective switching between cyclization-carbonylation and cyclization-carbonylation-cyclization-coupling (CCC-coupling) reactions of 2-alkynylanilines catalyzed by palladium(II). The use of a [Pd(tfa)$_2$(box)] catalyst in *i*PrOH afforded symmetrical ketones bearing two indoles in good yields; replacing the catalyst and solvent with Pd(tfa)$_2$ and DMSO/MeOH led to the formation of methyl 1-benzyl-1*H*-indole-3-carboxylates in good yields.

Introduction

Indoles are recognized as an important class of *N*-heterocycles in pharmaceutical science.[1] They constitute the core framework of a large variety of drugs and important biologically active compounds that occur in nature, such as vincristine (anti-cancer), panobinostat (anti-leukemic), tropisetron (antiemetic), vincamine (vasodilator), pindolol (antihypertensive), indomethacin (anti-inflammatory), atevirdine (anti-HIV), arbidol (antiviral), melatonin, tryptamine, serotonin (monoamine neurotransmitters), indole-3-acetic acid (auxin) and lysergic acid (Fig. 1).[2] Diarylketones are also frequently found in natural products and pharmaceuticals,[3] e.g., 3-aroyl indoles (anti-cancer),[3f] raloxifene (selective estrogen receptor modulator used for treatment of osteoporosis), benzbromarone (antipodagric) and amiodarone (antiarrhythmic). A variety of heterocycles can be synthesized by transition-metal-catalyzed cyclization of unsaturated systems.[4] 2-Alkynylanilines are good precursors for the synthesis of 3-substituted indoles.[5] Among these, indole-3-carboxylates are also an important class of heterocyclic compounds which display a wide range of biological activities.[5b] Gabriele et al. reported PdI$_2$-KI-catalyzed cyclization-carbonylation of *N*-benzyl 2-alkynylanilines, with indole-3-carboxylates obtained in 69–84% yields.[5b]

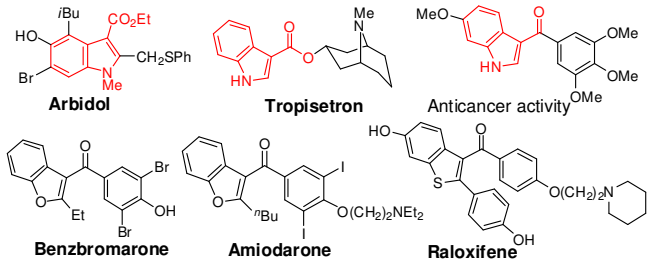
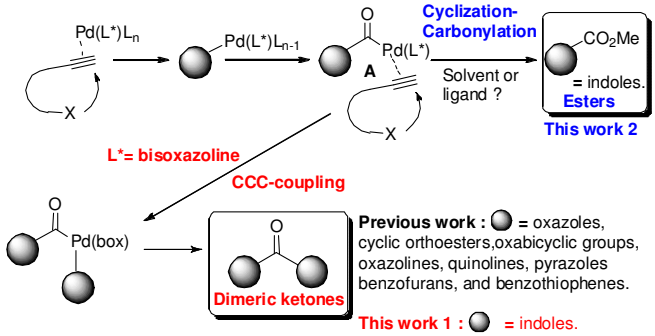


Fig. 1 Structures of biologically active indoles and diarylketones.

If these intramolecular cyclization-carbonylation reactions could be expanded to include carbonylative coupling reactions, the process would be a synthetically valuable method for direct



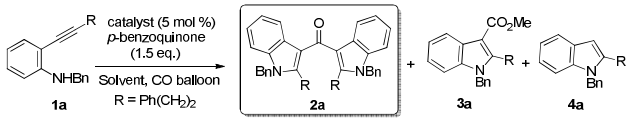
Scheme 1 Reaction courses of cyclization-carbonylation and cyclization-carbonylation-cyclization-coupling (CCC-coupling) in propargylic compounds.

preparation of ketones bearing two indole groups. Recently, we reported a cyclization-carbonylation-cyclization-coupling reaction (CCC-coupling reaction) of propargyl acetate, amides,[6a] γ-propynyl-1,3-diketones,[6b] *N*-propargylanilines, *o*-alkynylphenols,[6c] propargyl ureas,[6d] α,β-alkynic hydrazones[6e] and (*o*-alkynylphenyl) (methoxymethyl) sulfides[6f] catalyzed by palladium(II)-bisoxazoline (box) complexes (Scheme 1). Symmetrical ketones bearing two oxazoles, cyclic orthoesters, oxabicyclic groups, quinolines, benzofurans, oxazolines, pyrazoles and benzo[*b*]thiophenes were obtained in one-step reactions. In this transformation, the triple bond of the substrate coordinates to palladium(II) and undergoes nucleophilic attack by the intramolecular nucleophile X followed by CO insertion to produce the acyl palladium intermediate **A**. Coordination of the triple bond of a second molecule induces the second cyclization,[7] and reductive elimination then leads to the formation of a ketone bearing two heterocyclic groups. Meanwhile, methanolysis of the acyl palladium intermediate **A** gives the ester product as a result of cyclization-carbonylation. If the course of the reaction is switched by a simple change of ligand (or solvent), heterocycle-3-carboxylates and symmetrical ketones bearing two indole groups (dimeric ketones) are selectively synthesized. In this work, we investigated Pd(II)-catalyzed ligand-controlled switching

between cyclization-carbonylation and CCC-coupling reactions of 2-alkynylanilines.

Results and discussion

Table 1. Optimization of CCC-coupling reaction of **1a.**



Entry	Catalyst	Solvent	Temp (ºC), Time (h)	Yield of **2a** (%)	Yield of **3a** (%)	Yield of **4a** (%)
1	$Pd(tfa)_2$	MeOH	0 ~ rt, 48	-	41	-
2[a]	$[PdCl_2(Ph_3P)_2]$	MeOH	0 ~ rt, 48	-	34	17
3	$[PdCl_2(CH_3CN)_2]$	MeOH	0, 47	15	57	-
4	$[PdCl_2$(2,2'-bipy)]	MeOH	0 ~ rt, 51	33	5	53
5	$[Pd(tfa)_2$(2,2'-bipy)][b]	MeOH	0, 72	40	3	27
6	$[Pd(OAc)_2$(**L1**)]	MeOH	0 ~ rt, 72	18	24	20
7[d]	$[Pd(tfa)_2$(**L1**)][c]	MeOH	0, 72	20	13	-
8	$[Pd(tfa)_2$(**L2**)][b]	MeOH	-10, 69	79	8	15
9	$[Pd(tfa)_2$(**L3**)][b]	MeOH	0, 58	42	58	-
10	$[PdCl_2$(**L2**)][b]	MeOH	0, 72	49	8	31
11	$[Pd(tfa)_2$(**L2**)][b]	DMF	0, 72		NR	
12	$[Pd(tfa)_2$(**L2**)][b]	CH_2Cl_2	0, 72		NR	
13	$[Pd(tfa)_2$(**L2**)][b]	EtOH	0 ~ rt, 48	81	4	16
14	$[Pd(tfa)_2$(**L2**)][b]	*i*PrOH	0, 47	91	trace	trace
15	$[Pd(tfa)_2$(**L2**)][b]	*i*BuOH	0 ~ rt, 51	52	-	40

[a] Recovery 54%. [b] Isolated complex was employed. [c] $Pd(tfa)_2$ 5 mol % / **L1** 10 mol %. [d] Recovery 54%

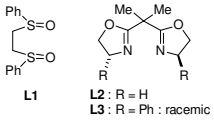
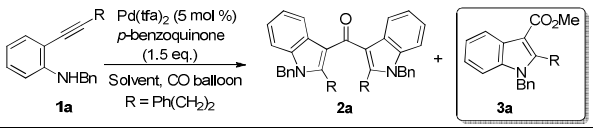


Fig. 2 Ligands for Table 1

Synthesis of the 2-alkynyl-*N*-benzylaniline substrates **1** was carried out from the appropriate 2-iodoanilines, which were converted to their *N*-benzyl derivatives using a reductive amination protocol. Sonogashira coupling of the *N*-benzyl-2-iodoanilines with terminal acetylenes, according to the literature, gave **1**.[8] Initially, we selected **1a** as a standard substrate to search for potential catalysts (Table 1, Fig. 2). The reaction of **1a** with $Pd(tfa)_2$ (5 mol%) and *p*-benzoquinone (1.5 equiv.) in methanol under a carbon monoxide atmosphere (balloon) afforded the indole-3-carboxylate derivative **3a** in 41% yield along with an unidentified mixture (Table 1, entry 1). The use of $[PdCl_2(PPh_3)_2]$ and $[PdCl_2(CH_3CN)_2]$ also gave the ester **3a** in yields of 34~57% as a major product (Table 1, entries 2 and 3). The desired ketone **2a** was obtained using palladium complexes bearing 2,2'-bipyridine and the sulfoxide ligand **L1**, although the yields were low (Table 1, entries 4–6). Next, an attempt was made to use the box-Pd^{II} complexes according to our previous results (Table 1, entries 7–10).[6,7] As expected, the reaction occurred smoothly in the presence of the $[Pd(tfa)_2$**L2**], and the yield of dimeric ketone **2a** improved to 79% (Table 1, entry 8). The nature of the counteranion of the palladium complexes had some influence on the catalytic activity (Table 1, entries 8 and 10). When the carbonylation reaction was started, substrate **1a** did not completely dissolve in methanol due to its high lipophilicity. Therefore, various solvents were tested in the carbonylation reaction. DMF and CH_2Cl_2 were not suitable as solvents, as the reaction did not proceed when they were used (Table 1, entries 11 and 12). Finally, 2-propanol was found to be the best solvent, affording the dimeric ketone **2a** in 91% yield (Table 1, entries 13–15). Next, we turned our attention to the synthesis of indole-3-carboxylate derivative **3a** (Table 2). A palladium(II)/DMSO catalytic system has been used in a variety of oxidative transformations, and DMSO has been proposed as a ligand.[9] Lee et al. reported Pd(II)-catalyzed controlled switching between oxidative Heck reaction and conjugate addition to enones.[10] In this reaction, DMSO plays a vital role in switching between two reaction pathways. Inspired by these studies, several different solvent mixtures at various ratios (DMSO/MeOH) were tested in the carbonylation reaction of **1a** (Table 2, entries 1–5). Although a large amount of DMSO (DMSO/MeOH = 5/1) led to decreased product yield (Table 2, entry 1), the best results were obtained by using the ratio DMSO/MeOH = 1/5 or 1/10 with $Pd(tfa)_2$, affording **3a** in 83–86% yields (Table 2, entries 4–7). In addition, the use of other mixed solvents (THF/MeOH, CH_2Cl_2/MeOH and DMF/MeOH) did not give good results (Table 2, entries 8–10).

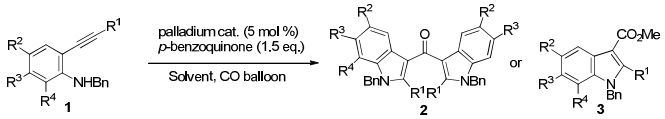
Table 2. Optimization of cyclization-carbonylation reaction of **1a.**



Entry	Solvent	Temp (ºC), Time (h)	Yield of **2a** (%)	Yield of **3a** (%)	Recovery of **1a** (%)
1	DMSO / MeOH = 5 / 1	0 ~ rt, 48	-	5	78
2	DMSO / MeOH = 1 / 1	0, 72	-	71	21
3[a]	DMSO / MeOH = 1 / 1	0, 72	14	34	40
4	DMSO / MeOH = 1 / 2	0 ~ 5, 72	-	74	12
5	DMSO / MeOH = 1 / 5	0, 72	-	86	5
6	DMSO / MeOH = 1 / 10	0 ~ 5, 72	-	83	7
7	DMSO / MeOH = 1 / 21	0, 48	-	82	4
8	THF / MeOH = 1 / 1	0, 72	-	57	37
9	CH_2Cl_2 / MeOH = 1 / 1	0, 72	-	51	33
10	DMF / MeOH = 1 / 1	0, 72	-	52	21

[a] $PdCl_2$ was employed as a catalyst.

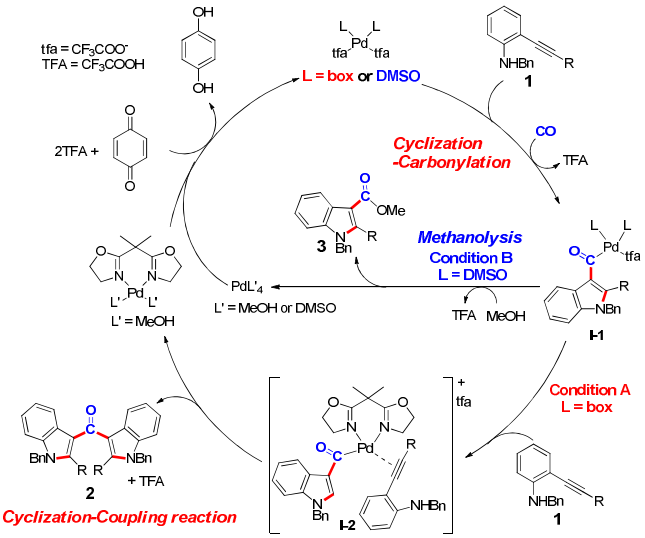
Table 3. Substrate scope of CCC-coupling (condition A) and cyclization-carbonylation reactions (condition B).



Condition A : [Pd(tfa)$_2$(**L2**)], *i*PrOH (for entries 1-18, Table3). **L2** = 2,2'-isopropylidenebisoxazoline.
Condition B : Pd(tfa)$_2$, DMSO / MeOH = 1 / 5 (for entries 19-30, Table3).

Entry	R^1	R^2	R^3	R^4	Temp (°C) , Time (h)	Yield (%)
1	$Ph(CH_2)_2$	H	H	H	0, 47	**2a** : 91
2	$Me(CH_2)_3$	H	H	H	0, 72	**2b** : 89
3	$Me(CH_2)_7$	H	H	H	0, 72	**2c** : 90
4	Ph	H	H	H	0 ~ rt, 72	**2d** : 86
5	4-MeOPh	H	H	H	-5 ~ 5, 72	**2e** : 89
6	4-CF_3Ph	H	H	H	0 ~ rt, 72	**2f** : 83
7	4-FPh	H	H	H	15, 48	**2g** : 87
8	4-ClPh	H	H	H	15, 72	**2h** : 84
9	4-BrPh	H	H	H	0 ~ rt, 72	**2i** : 92
10	4-MePh	H	H	H	15, 48	**2j** : 82
11	4-*t*BuPh	H	H	H	0 ~ 15, 72	**2k** : 89
12	$Ph(CH_2)_2$	Br	H	H	0, 72	**2l** : 74
13	Ph	Me	H	H	5 ~ 10, 72	**2m** : 89
14	Ph	Me	H	Me	0, 48	**2n** : 86
15	$Ph(CH_2)_2$	H	MeO	H	5, 72	**2o** : 76
16	Ph	H	MeO	H	0 ~ rt, 72	**2p** : 76
17	3,5-$(MeO)_2$Ph	H	H	H	5 ~ 15, 72	**2q** : 73
18	3,4,5-$(MeO)_3$Ph	H	H	H	0 ~ 15, 72	**2r** : 76
19	$Ph(CH_2)_2$	H	H	H	0, 72	**3a** : 86
20	$Me(CH_2)_3$	H	H	H	0, 72	**3b** : 79
21	$Me(CH_2)_7$	H	H	H	0, 72	**3c** : 79
22	Ph	H	H	H	0, 72	**3d** : 82
23	4-MeOPh	H	H	H	0, 48	**3e** : 74
24	4-CF_3Ph	H	H	H	0 ~ rt, 120	**3f** : 85
25	4-FPh	H	H	H	0 ~ rt, 72	**3g** : 89
26	4-ClPh	H	H	H	0 ~ rt, 72	**3h** : 87
27	4-BrPh	H	H	H	0 ~ 15, 48	**3i** : 83
28	4-MePh	H	H	H	15, 48	**3j** : 90
29	4-*t*BuPh	H	H	H	0 ~ 10, 72	**3k** : 84
30	Ph	Me	H	H	0, 72	**3m** : 85
31	Ph	Me	H	Me	0, 48	**3n** : 78
32	H	H	H	H	0, 48	**3s** : 80

Having elucidated the optimum conditions for both reactions, we then employed a variety of 2-alkynylanilines **1** in the CCC-coupling reaction (Table 3, entries 1–18, condition A). Substrates **1a**–**1d**, bearing alkyl and phenyl substituents at the alkyne terminus, gave good results which were similar to that of the parent substrate **1a** (Table 3, entries 1–4). Substrates **1e** and **1f**, bearing both electron-donating and electron-withdrawing substituents on an aromatic moiety in the alkyne terminus, afforded the products **2e** and **2f** in 83~89% yields (Table 3, entries 5 and 6). The three kinds of halogen substituent (F, Cl, Br) and alkyl groups on the phenyl ring in the alkyne terminus were tolerated under the reaction conditions used (Table 3, entries 7–11). Substrates **1l**–**1n**, bearing Br and methyl groups on the aniline ring, were transformed to the corresponding ketones **2l**–**2n** in 74–89% yields (Table 3, entries 12–14). The introduction of methoxy groups on the aniline ring led to a slightly lowered yield (Table 3, entries 15–16). Substrates **1q**–**1r**, bearing two or three methoxy groups on the phenyl ring at the alkyne terminus, afforded the products **2q**–**2r** in 73–76% yields (Table 3, entries 17–18). The reaction pathways were switched by using condition B. Substrates **1a**–**1d**, bearing alkyl and phenyl substituents at the alkyne terminus, were transformed to the corresponding methyl indole-3-carboxylates **3a**–**3d** in good yields (Table 3, entries 19–22). Substrates **1e** and **1f**, bearing both electron-donating and electron-withdrawing substituents on an aromatic moiety in the alkyne terminus, gave moderate to good results (Table 3, entries 23 and 24). The three kinds of halogen substituent (F, Cl, Br) and alkyl groups on the phenyl ring in the alkyne terminus were tolerated under the reaction conditions used (Table 3, entries 25–29). Substrates **1m** and **1n**, bearing methyl groups on the aniline ring, were transformed to the corresponding esters **2m** and **2n** in 85 and 78% yield, respectively (Table 3, entries 30 and 31). It is noteworthy that the terminal acetylene **1s** was transformed to **3s** in 80% yield (Table 3, entry 32).



Scheme 2 Plausible mechanism for the CCC-coupling and cyclization-carbonylation reactions of **1**.

A plausible mechanism for the CCC-coupling and cyclization-carbonylation reactions of **1** is shown in Scheme 2. Nucleophilic attack by the nitrogen atom at the electrophilically activated triple bond is followed by CO insertion to produce the acyl palladium intermediate **I-1**. Under condition A (L = box), coordination of the triple bond of a second molecule (**I-2**) induces the second cyclization, and reductive elimination then leads to the formation of a ketone bearing two indole groups. We believe that the box ligand enhances the π-electrophilicity of palladium(II),[7] and thus promotes coordination of the second triple bond to the acyl

palladium intermediate **I-1**, leading to the dimerization reaction. Under condition B, DMSO acts as a neutral ligand instead of a box.[11] Methanolysis of the acyl palladium intermediate **I-1** should be facilitated, giving indole-3-carboxylates **3** in good yields.

Conclusions

In conclusion, we developed an efficient way of switching between CCC-coupling and cyclization-carbonylation reactions of 2-alkynylanilines (**1**) catalyzed by Pd^{II}. The use of $[Pd(tfa)_2(box)]$ as a catalyst in *i*PrOH afforded symmetrical ketones bearing two indoles in good to excellent yields, while replacing the catalyst and solvent with $Pd(tfa)_2$ and DMSO/MeOH led to the formation of methyl 1-benzyl-1*H*-indole-3-carboxylates in good yields. These reactions were general for a wide range of 2-alkynylanilines. We are currently investigating additional cascade reactions based on the reaction strategy of CCC-coupling and cyclization-carbonylation presented here for the synthesis of the other types of ketone containing two heterocyclic groups and heterocycles-carboxylates.

Experimental Section

General Information.

See Supporting Information for general experimental details as well as procedures for the preparation and characterization of all precursors and products.

Preparation of box-palladium complexes.

The box ligands **L1~L3** and palladium complexes $[Pd(tfa)_2(2,2'\text{-bipy})]$, $[Pd(tfa)_2(\mathbf{L2})]$, $[Pd(tfa)_2(\mathbf{L3})]$ and $[PdCl_2(\mathbf{L3})]$ were prepared according to the literature.[6a,6d,12]

Typical procedure for CCC-coupling reaction of *N*-benzyl-2-(4-phenylbut-1-yn-1-yl)aniline (1a) : Condition A

A 30-mL two-necked round-bottom flask containing a magnetic stirring bar, *N*-benzyl-2-(4-phenylbut-1-yn-1-yl)aniline (**1a**) (100 mg, 0.32 mmol), *p*-benzoquinone (51.9 mg, 0.48 mmol) and MeOH (3 mL) was fitted with a rubber septum and a three-way stopcock connected to a balloon filled with carbon monoxide. The apparatus was purged with carbon monoxide by pump-filling via the three-way stopcock. A MeOH (1 mL) solution (or suspension) of catalyst was added to the stirred solution via syringe at 0°C. The remaining catalyst was washed in MeOH (1 mL) twice, and stirred for 47 h at the same temperature. In most cases, the dimeric ketones precipitated from the reaction mixture. The resulting precipitate was collected by filtration and washed with cold MeOH (1.5 mL × 2) to yield dimeric ketone **2a**. As small amounts of **2a** (and **3a**, see Table 1) still remained in the filtrate, the filtrate was diluted with CH_2Cl_2 (50 mL) and washed with 5% NaOH (40 mL). The aqueous layer was extracted with CH_2Cl_2 (25 mL) and the combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by column chromatography on silica gel. The fraction eluted with hexane/ethyl acetate (20/1) afforded small amounts of dimeric ketone **2a** (monomeric ester **3a**, hexane/ethyl acetate = 50/1).

*Bis(1-benzyl-2-phenethyl-1H-indol-3-yl)methanone (**2a**):* 91% yield (93.9 mg), white solid, mp 139-141°C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.83-2.90 (4H, m), 3.16-3.28 (4H, m), 5.25 (4H, s), 6.97-7.03 (10H, m), 7.10-7.28 (16H, m), 7.41 (2H, br-d, J = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.2 (2C), 36.7 (2C), 46.5 (2C), 109.8 (2C), 116.9 (2C), 120.9 (2C), 121.3 (2C), 122.2 (2C), 125.9 (4C), 126.1 (2C), 126.8 (2C), 127.6 (2C), 128.4 (4C), 128.4 (4C), 128.9 (4C), 136.4(2C), 136.9 (2C), 141.0 (2C), 145.2 (2C), 188.3; IR (KBr) 1614, 1604, 1523, 1455, 1410 cm^{-1}; HRMS-EI: *m/z* [M$^+$] calcd for $C_{47}H_{40}N_2O$ 648.3141, found 648.3141.

*Bis(1-benzyl-2-butyl-1H-indol-3-yl)methanone (**2b**):* 89% yield (93.5 mg) from **1b** (100 mg, 0.38 mmol), white soild, mp ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.78 (6H, t, J = 7.2 Hz), 1.26-1.32 (4H, m), 1.50-1.56 (4H, m), 2.92-2.98 (4H, m), 5.42 (4H, s), 6.97 (2H, t, J = 7.6 Hz), 7.05-7.11 (6H, m), 7.20-7.33 (8H, m), 7.37 (2H, br-d, J = 8.4Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.7 (2C), 22.8 (2C), 25.3 (2C), 32.5 (2C), 46.7 (2C), 109.7 (2C), 116.8 (2C), 120.8 (2C), 121.1 (2C), 121.9 (2C), 126.0 (4C), 127.1 (2C), 127.6 (2C), 128.9 (4C), 136.3 (2C), 137.0 (2C), 146.3 (2C), 188.5; IR (KBr) 2956, 1603, 1522, 1463, 1410 cm^{-1}; HRMS-EI: *m/z* [M$^+$] calcd for $C_{39}H_{40}N_2O$ 552.3141, found 552.3142.

*Bis(1-benzyl-2-octyl-1H-indol-3-yl)methanone (**2c**):* 90% yield (92.6 mg) from **1c** (100 mg, 0.31 mmol), white soild, mp ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.83 (6H, t, J = 6.8 Hz), 1.13-1.25 (20H, m), 1.50-1.58 (4H, m), 2.90-2.98 (4H, m), 5.42 (4H, s), 6.97 (2H, br-t, J = 8.0 Hz), 7.04-7.11 (6H, m), 7.20-7.32 (8H, m), 7.38 (2H, br-d, J = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1 (2C), 22.6 (2C), 25.6 (2C), 29.2 (2C), 29.2 (2C), 29.7 (2C), 30.5 (2C), 31.8 (2C), 46.7 (2C), 109.7 (2C), 116.8 (2C), 120.8 (2C), 121.1 (2C), 121.9 (2C), 125.9 (4C), 127.1 (2C), 127.6 (2C), 128.9 (4C), 136.3 (2C), 137.0 (2C), 146.4 (2C), 188.5; IR (KBr) 2924, 1604, 1523, 1464, 1410 cm^{-1}; HRMS-EI: *m/z* [M$^+$] calcd for $C_{47}H_{56}N_2O$ 664.4393, found 664.4392.

*Bis(1-benzyl-2-phenyl-1H-indol-3-yl)methanone (**2d**):* 86% yield (89.0 mg) from **1d** (100 mg, 0.35 mmol), yellow soild, mp 295-297°C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.04 (4H, s), 6.64-6.67 (4H, m), 6.96-7.03 (10H, m), 7.11-7.27 (12H, m), 8.06 (2H, br-d, J = 7.2Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 47.7 (2C), 110.3 (2C), 118.3 (2C), 121.1 (2C), 121.9 (2C), 122.9 (2C), 125.7 (4C), 127.2 (2C), 127.4 (4C), 128.0 (2C), 128.2 (2C), 128.6 (4C), 130.1 (2C), 130.5 (4C), 136.9 (2C), 137.3 (2C), 143.9 (2C), 189.2; IR (KBr) 1604, 1484, 1461, 1450, 1418, 1143 cm^{-1}; HRMS-EI: *m/z* [M$^+$] calcd for calcd for $C_{43}H_{32}N_2O$ 592.2515, found 592.2513.

*Bis(1-benzyl-2-(4-methoxyphenyl)-1H-indol-3-yl)methanone (**2e**):* 89% yield (93.0 mg) from **1e** (100 mg, 0.32 mmol), yellow soild, mp 220-223°C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.64 (6H, s), 5.02 (4H, s), 6.50 (4H, d, J = 8.8 Hz), 6.68 (4H, d, J = 6.8 Hz), 6.89-6.94 (6H, m), 7.10-7.32 (10H, m), 8.10 (2H, d, J = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 47.8 (2C), 55.2 (2C), 110.2 (4C), 112.9 (4C), 117.8 (2C), 121.0 (2C), 121.8 (2C), 122.3 (2C), 122.7 (2C), 125.6 (4C), 127.2 (2C), 128.3 (2C), 128.7 (4C), 131.8 (2C), 137.1 (2C), 137.4 (2C), 144.0 (2C), 159.7 (2C), 189.6; IR (KBr) 1609,1496, 1460, 1251, 1177, 1030 cm^{-1}; HRMS-EI: *m/z* [M$^+$] calcd for calcd for $C_{45}H_{36}N_2O_3$ 652.2726, found 652.2726.

*Bis(1-benzyl-2-(4-(trifluoromethyl)phenyl)-1H-indol-3-yl)methanone (**2f**):* 83% yield (84.7 mg) from **1f** (100 mg, 0.28 mmol), yellow soild, mp 221-223°C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.05 (4H, br-s), 6.72-6.75 (4H, m), 7.06-7.08 (2H, m), 7.16-7.26 (14H, m), 7.33 (4H, d, J = 8.0 Hz), 7.88-7.91 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 47.9 (2C), 110.6 (2C), 119.1 (2C), 121.2 (2C), 122.3 (2C), 123.7 (2C), 123.8 (2C, q, $^1J_{C\text{-}F}$ = 270.8 Hz), 124.3 (4C, q, $^3J_{C\text{-}F}$ = 3.8 Hz), 125.5 (4C), 127.4 (2C), 127.6 (2C), 128.9 (4C), 130.3 (2C, q, $^2J_{C\text{-}F}$ = 32.4 Hz), 130.6 (4C), 133.9 (2C), 136.7 (2C), 137.1 (2C), 142.2 (2C), 188.1; IR (KBr) 1616, 1603, 1497, 1414, 1322, 1133 cm^{-1}; HRMS-EI: *m/z* [M$^+$] calcd for calcd for $C_{45}H_{30}N_2OF_6$ 728.2262, found 728.2263.

*Bis(1-benzyl-2-(4-fluorophenyl)-1H-indol-3-yl)methanone (**2g**):* 87% yield (90.5 mg) from **1g** (100 mg, 0.33 mmol), white soild, mp 108-110°C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.03 (4H, br-s), 6.67-6.72 (8H, m), 6.93-6.97 (4H, m), 7.03 (2H, d, J = 8.2 Hz),

7.15-7.32 (10H, m), 8.04 (2H, d, J = 8.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 47.7 (2C), 110.3 (2C), 114.5 (4C, d, $^2J_{C\text{-}F}$ = 21.9 Hz), 118.2 (2C), 121.1 (2C), 122.1 (2C), 123.3 (2C), 125.5 (4C), 126.1 (2C, d, $^4J_{C\text{-}F}$ = 3.9 Hz), 127.4 (2C), 127.7 (2C), 128.8 (4C), 132.2 (4C, d, $^3J_{C\text{-}F}$ = 8.6 Hz), 137.0 (2C), 137.0 (2C), 142.7(2C), 162.7 (2C, d, $^1J_{C\text{-}F}$ = 247.9 Hz), 188.7; IR (KBr) 1605, 1495, 1460, 1454, 1415, 1225 cm^{-1}; HRMS-EI: *m/z* [M$^+$] calcd for calcd for $C_{43}H_{30}F_2N_2O$ 628.2326, found 628.2324.

*Bis(1-benzyl-2-(4-chlorophenyl)-1H-indol-3-yl)methanone (**2h**):* 84% yield (86.3 mg) from **1h** (100 mg, 0.31 mmol), yellow soild, mp 140-144°C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.03 (4H, br-s), 6.69 (4H, br-d, *J*= 7.2 Hz), 6.90-6.92 (4H, m), 6.97-7.00 (4H, m), 7.03 (2H, br-d, *J*= 8.0 Hz), 7.17-7.21 (2H, m), 7.23-7.28 (4H, m), 7.33-7.37 (4H, m), 8.04 (2H, br-d, *J*= 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 47.9 (2C),110.4 (2C), 118.5 (2C), 121.1 (2C), 122.2 (2C), 123.5 (2C), 125.4 (4C), 127.4 (2C), 127.7 (4C), 127.8 (2C), 128.5 (2C), 129.0 (4C), 131.5 (4C), 134.6 (2C), 137.0 (2C), 137.2 (2C), 142.6 (2C), 188.7; IR (KBr) 1603, 1482, 1459, 1454, 1417 cm^{-1}; HRMS-EI: *m/z* [M$^+$] calcd for calcd for $C_{43}H_{30}N_2OCl_2$ 660.1735, found 660.1739.

*Bis(1-benzyl-2-(4-bromophenyl)-1H-indol-3-yl)methanone (**2i**):* 92% yield (96.6 mg) from **1i** (100 mg, 0.28 mmol), yellow soild, mp 254-255°C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.02 (4H, br-s), 6.50 (4H, br-d, *J* = 7.2 Hz), 6.84-6.87 (4H, m), 7.04 (2H, br-d, *J* = 8.0 Hz), 7.13-7.28 (10H, m), 7.35-7.39 (4H, m), 8.02 (2H, br-d, *J* = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 47.9 (2C), 110.4 (2C), 118.5 (2C), 121.1 (2C), 122.2 (2C), 122.9 (2C), 123.5 (2C), 125.4 (4C), 127.4 (2C), 127.8 (2C), 129.0 (2C), 129.0 (4C), 130.6 (4C), 131.7 (4C), 137.0 (2C), 137.3 (2C), 142.7 (2C), 188.7; IR (KBr) 1604, 1459, 1417, 1141, 1011 cm^{-1}; HRMS-EI: *m/z* [M$^+$] calcd for calcd for $C_{43}H_{30}N_2OBr_2$ 748.0725, found 748.0720.

*Bis(1-benzyl-2-(4-methylphenyl)-1H-indol-3-yl)methanone (**2j**):* 82% yield (86.8 mg) from **1j** (100 mg, 0.34 mmol), yellow soild, mp 137-138°C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.26 (6H, s), 5.03 (4H, s), 6.72-6.74 (4H, m), 6.84 (4H, d, *J* = 8.4 Hz), 6.93-6.95 (6H, m), 7.08-7.28 (10H, m), 8.01 (2H, br-d, *J* = 7.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$, one quaternary carbon peak (2C) was overlapped) δ 21.3 (2C), 47.8 (2C),110.2 (2C), 118.2 (2C), 121.1 (2C), 121.7 (2C), 122.7 (2C), 125.7 (4C), 127.1 (2C), 127.3 (2C), 128.1 (4C), 128.6 (4C), 130.3 (4C), 137.0 (2C), 137.5 (2C), 138.1 (2C), 144.3 (2C), 189.3; IR (KBr) 1603, 1454, 1412, 1141, 1059 cm^{-1}; HRMS-EI: *m/z* [M$^+$] calcd for calcd for $C_{45}H_{36}N_2O$ 620.2828, found 620.2829.

*Bis(1-benzyl-2-(4-(tert-butyl)phenyl)-1H-indol-3-yl)methanone (**2k**):* 89% yield (91.2 mg) from **1k** (100 mg, 0.29 mmol), yellow soild, mp 264-265°C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.19 (18H, s), 5.09 (4H, s), 6.84 (4H, br-d, *J* = 8.0 Hz), 6.95 (2H, d, *J* = 8.0 Hz), 7.04-7.13 (12H, m), 7.20-7.24 (6H, m), 7.84 (2H, br-d, *J* = 7.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.2 (6C), 34.5 (2C), 47.7 (2C),110.2 (2C), 118.7 (2C), 121.1 (2C), 121.5 (2C), 122.5 (2C), 124.2 (4C), 125.9 (4C), 127.2 (2C), 127.3 (2C), 127.8 (2C), 128.6 (4C), 130.0 (4C), 136.6 (2C), 137.4 (2C), 144.4 (2C), 151.2 (2C), 189.3; IR (KBr) 2963, 1619, 1608, 1496, 1460, 1410, 732 cm^{-1}; HRMS-EI: *m/z* [M$^+$] calcd for calcd for $C_{51}H_{48}N_2O$ 704.3767, found 704.3769.

*Bis(1-benzyl-5-bromo-2-phenethyl-1H-indol-3-yl)methanone (**2l**):* 74% yield (77.6 mg) from **1l** (100 mg, 0.26 mmol), yellow soild, mp 78-80°C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.84-2.89 (4H, m), 3.16-3.22 (4H, m), 5.20 (4H, s), 6.91-7.00 (8H, m), 7.08 (2H, d, *J* = 8.4 Hz), 7.12-7.34 (14H, m), 7.52 (2H, d, *J* = 1.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.1 (2C), 36.5 (2C), 46.7 (2C), 111.5 (2C), 115.1 (2C), 116.1 (2C), 123.2 (2C), 125.3 (2C), 125.7 (4C), 126.3 (2C), 127.8 (2C), 128.4 (6C), 128.5 (4C), 129.2 (4C), 135.0 (2C), 136.2 (2C), 140.5 (2C), 146.1 (2C), 187.1; IR (KBr) 1601, 1522, 1508, 1457, 1437, 1411 cm^{-1}; HRMS-ESI$^+$ m/z [M+Na]$^+$ Calcd for $C_{47}H_{38}Br_2N_2NaO$ 827.1249 found 827.1278.

*Bis(1-benzyl-5-methyl-2-phenyl-1H-indol-3-yl)methanone (**2m**):* 89% yield (94.0 mg) from **1m** (100 mg, 0.34 mmol), yellow soild, mp >300°C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.45 (6H, s), 5.02 (4H, s), 6.69-6.71 (4H, m), 6.85 (2H, d, *J* = 8.4 Hz), 6.94 (2H, dd, *J* = 8.4, 1.6 Hz), 7.02-7.04 (8H, m), 7.19-7.26 (8H, m), 7.85 (2H, br-s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.6 (2C), 47.7 (2C), 109.9 (2C), 117.9 (2C), 121.0 (2C), 124.4 (2C), 125.8 (4C), 127.2 (2C), 127.3 (4C), 128.1 (2C), 128.2 (2C), 128.6 (4C), 130.4 (2C), 130.5 (4C), 131.2 (2C), 135.3 (2C), 137.5 (2C), 144.0(2C), 188.9; IR (KBr) 1604, 1476, 1410, 1351, 1055 cm^{-1}; HRMS-EI: *m/z* [M$^+$] calcd for calcd for $C_{45}H_{36}N_2O$ 620.2828, found 620.2827.

*Bis(1-benzyl-5,7-dimethyl-2-phenyl-1H-indol-3-yl)methanone (**2n**):* 86% yield (89.3 mg) from **1n** (100 mg, 0.32 mmol), yellow soild, mp 127-129°C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.28 (6H, s), 2.38 (6H, s), 5.20 (4H, br-s), 6.58 (4H, br-d, *J* = 6.0 Hz), 6.70 (2H, br-s), 7.03-7.07 (8H, m), 7.19-7.25 (8H, m), 7.67 (2H, br-s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.4 (2C), 21.2 (2C), 48.9 (2C), 118.3 (2C), 119.0 (2C), 120.3 (2C), 125.1 (4C), 126.9 (4C), 127.2 (4C), 127.7 (2C), 128.0 (2C), 128.7 (4C), 128.9 (2C), 130.5 (2C), 130.8 (2C), 131.0 (2C), 133.9 (2C), 139.8 (2C), 144.6 (2C), 189.0; IR (KBr) 1600, 1484, 1421, 1396, 703 cm^{-1}; HRMS-EI: *m/z* [M$^+$] calcd for calcd for $C_{47}H_{40}N_2O$ 648.3141, found 648.3139.

*Bis(1-benzyl-6-methoxy-2-phenethyl-1H-indol-3-yl)methanone (**2o**):* 76% yield (78.1 mg) from **1o** (100 mg, 0.29 mmol), yellow soild, mp 156-157°C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.81-2.88 (4H, m), 3.15-3.22 (4H, m), 3.75 (6H, s), 5.20 (4H, s), 6.65-6.70 (4H, m), 6.98-7.04 (8H, m), 7.11-7.30 (14H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.2 (2C), 36.9 (2C), 46.5 (2C), 55.6 (2C), 93.8 (2C), 110.4 (2C), 116.8 (2C), 121.1 (2C), 121.7 (2C), 126.0 (4C), 126.1 (2C), 127.6 (2C), 128.4 (8C), 129.0 (4C), 136.9 (2C), 137.2(2C), 141.1 (2C), 144.2 (2C), 156.4 (2C), 188.2; IR (KBr) 1598, 1523, 1453, 1404, 1150 cm^{-1}; HRMS-EI: *m/z* [M$^+$] calcd for calcd for $C_{49}H_{44}N_2O_3$ 708.3352, found 708.3353.

*Bis(1-benzyl-6-methoxy-2-phenyl-1H-indol-3-yl)methanone (**2p**):* 76% yield (79.4 mg) from **1p** (100 mg, 0.32 mmol), yellow soild, mp 126-128°C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.72 (6H, s), 4.97 (4H, s), 6.40 (2H, d, *J* = 2.4 Hz), 6.64-6.66 (4H, m), 6.88 (2H, dd, *J* = 2.4, 8.8 Hz), 6.95-7.03 (8H, m), 7.18-7.26 (8H, m) 7.95 (2H, d, *J* = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 47.8 (2C), 55.6 (2C), 94.1 (2C), 111.0 (2C), 118.3 (2C), 121.9 (2C), 122.4 (2C), 125.8 (4C), 127.2 (2C), 127.4 (4C), 128.0 (2C), 128.7 (4C), 130.2 (2C), 130.4 (4C), 137.2 (2C), 137.9 (2C), 143.1 (2C), 156.8 (2C), 189.4; IR (KBr) 1606, 1491, 1049, 818 cm^{-1}; HRMS-EI: *m/z* [M$^+$] calcd for calcd for $C_{45}H_{36}N_2O_3$ 652.2726 found 652.2725.

*Bis(1-benzyl-2-(3,5-dimethoxyphenyl)-1H-indol-3-yl)methanone (**2q**):* 73% yield (75.5 mg) from **1q** (100 mg, 0.29 mmol), yellow soild, mp 132-134°C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.22 (12H, s), 5.10 (4H, br-s), 6.10 (4H, d, *J* = 2.4 Hz), 6.31 (2H, t, *J* = 2.4 Hz), 6.76 (4H, d, *J* = 7.6 Hz), 7.04 (2H, d, *J* = 8.0 Hz), 7.17-7.31 (10H, m), 8.15 (2H, t, *J* = 7.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 48.1 (2C), 54.8 (4C), 102.6 (2C), 108.1 (4C), 110.4(2C), 118.1 (2C), 121.3 (2C), 122.0 (2C), 123.3 (2C), 125.5 (4C), 127.1 (2C), 128.2 (2C), 128.8 (4C), 131.5 (2C), 137.3 (2C), 137.5 (2C), 143.9 (2C), 159.4 (4C), 189.3; IR (KBr): 1596, 1464, 1455, 1419, 1206, 1155 cm^{-1}; HRMS-ESI$^+$ m/z [M+H]$^+$ Calcd for $C_{47}H_{41}N_2O_5$ 713.3015 found 713.3019.

*Bis(1-benzyl-2-(3,4,5-trimethoxyphenyl)-1H-indol-3-yl)methanone (**2r**):* 76% yield (79.3 mg) from **1r** (100 mg, 0.27 mmol), yellow soild, mp 227-230°C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.07 (12H, s), 3.74 (6H, s), 5.10 (4H, br-s), 6.13 (4H, s), 6.74 (4H, d, *J* = 7.6 Hz), 7.05 (2H, d, *J* = 8.0 Hz), 7.16-7.29 (6H, m), 7.37 (4H, t, *J* = 7.6 Hz), 8.24 (2H, d, *J* = 7.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 48.4 (2C), 55.3 (4C), 60.7 (2C), 108.1 (4C), 110.4(2C), 117.8 (2C), 121.2 (2C), 122.2 (2C), 123.5 (2C), 124.9 (2C), 125.1 (4C), 127.3 (2C), 128.4 (2C), 129.2 (4C), 137.5 (2C), 137.7 (2C), 138.2 (2C), 144.0 (2C), 151.9 (4C), 189.5; IR (KBr)

1583, 1496, 1454, 1418, 1240, 1126 cm^{-1}; HRMS-ESI$^+$ m/z $[M+Na]^+$ Calcd for $C_{49}H_{44}N_2NaO_7$ 795.3046 found 795.3065.

Typical procedure for cyclization-carbonylation reaction of *N*-benzyl-2-(4-phenylbut-1-yn-1-yl)aniline (1a) : Condition B

A 30-mL two-necked round-bottom flask containing a magnetic stirring bar, *N*-benzyl-2-(4-phenylbut-1-yn-1-yl)aniline (**1a**) (100 mg, 0.32 mmol), *p*-benzoquinone (51.9 mg, 0.48 mmol) and MeOH (8 mL) was fitted with a rubber septum and a three-way stopcock connected to a balloon filled with carbon monoxide. The apparatus was purged with carbon monoxide by pump-filling via the three-way stopcock. A DMSO (1 mL) solution of catalyst was added to the stirred solution via syringe at 0°C. The remaining catalyst was washed in DMSO (2 mL) and MeOH (2 mL) and stirred for 72 h at the same temperature. The mixture was diluted with CH_2Cl_2 (70 mL) and washed with 5% NaOH (40 mL). The aqueous layer was extracted with CH_2Cl_2 (25 mL) and the combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by column chromatography on silica gel. The fraction eluted with hexane/ethyl acetate (50/1) afforded monomeric ester **3a**.

*Methyl 1-benzyl-2-phenethyl-1H-indole-3-carboxylate (**3a**):* 86% yield (102.0 mg) from **1a** (100 mg, 0.32 mmol), yellow soild, mp 90-91°C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.82-2.86 (2H, m), 3.37-3.41 (2H, m), 3.97 (3H, s), 5.11 (2H, s), 6.91-6.94 (2H, m), 7.10-7.12 (2H, m), 7.18-7.27 (9H, m), 8.20 (1H, br-d, J = 1.2, 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.5, 35.8, 46.3, 50.8, 104.2, 109.8, 121.6, 122.0, 122.5, 125.9 (2C), 126.3, 126.6, 127.7, 128.5 (2C), 128.5 (2C), 128.9 (2C), 136.3, 136.6, 141.1, 148.6, 166.1; IR (KBr) 1685, 1530, 1443, 1235, 1113 cm^{-1}; HRMS-EI: *m/z* $[M^+]$ calcd for $C_{25}H_{23}NO_2$ 369.1729, found 369.1731.

*Methyl 1-benzyl-2-butyl-1H-indole-3-carboxylate (**3b**)* [13a] *:* 79% yield (96.8 mg) from **1b** (100 mg, 0.38 mmol).

*Methyl 1-benzyl-2-octyl-1H-indole-3-carboxylate (**3c**):* 79% yield (92.7 mg) from **1c** (100 mg, 0.31 mmol), yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.86 (3H, t, J = 6.8 Hz), 1.23-1.59 (12H, m), 3.12-3.16 (2H, m), 3.94 (3H, s), 5.37 (2H, s), 6.95-6.98 (2H, m), 7.16-7.27 (6H, m), 8.16 (1H, br-d, J = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 22.6, 25.8, 29.2, 29.3, 29.6, 29.8, 31.8, 46.6, 50.7, 103.9, 109.9, 121.6, 121.9, 122.3, 125.8 (2C), 126.8, 127.6, 128.9 (2C), 136.3, 136.6, 149.9, 166.2; IR (KBr) 2925, 1698, 1535, 1464, 1139, 1114 cm^{-1}; HRMS-EI: *m/z* $[M^+]$ calcd for $C_{25}H_{31}NO_2$ 377.2355, found 377.2356.

*Methyl 1-benzyl-2-phenyl-1H-indole-3-carboxylate (**3d**)* [13a]*:* 82% yield (98.4 mg) from **1d** (100 mg, 0.35 mmol).

*Methyl 1-benzyl-2-(4-methoxyphenyl)-1H-indole-3-carboxylate (**3e**):* 74% yield (88.0 mg) from **1e** (100 mg, 0.32 mmol), Yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.79 (3H, s), 3.83 (3H, s), 5.20 (2H, s), 6.90-6.94 (4H, m), 7.20-7.31 (8H, m), 8.25 (1H, br-d, J = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 47.5, 50.8, 55.2, 105.4, 110.7, 113.6 (2C), 122.0, 122.2, 123.0, 123.1, 126.0 (2C), 126.8, 127.4, 128.7 (2C), 131.5 (2C), 136.3, 137.0, 147.2, 160.1, 165.7; IR (KBr) 1701, 1686, 1459, 1250, 1149 cm^{-1}; HRMS-EI: *m/z* $[M^+]$ calcd for $C_{24}H_{21}NO_3$: 371.1521; found: 371.1521.

*Methyl 1-benzyl-2-(4-(trifluoromethyl)phenyl)-1H-indole-3-carboxylate (**3f**):* 85% yield (97.4 mg) from **1f** (100 mg, 0.28 mmol), yellow solid, mp 122-124°C, ^{1}H NMR (400. MHz, $CDCl_3$) δ 3.78 (3H, s), 5.18 (2H, s), 6.87-6.89 (2H, m), 7.23-7.35 (6H, m), 7.46 (2H, d, J = 8.0 Hz), 7.66 (2H, d, J = 8.0 Hz), 8.27 (1H, br-d, J = 7.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 47.6, 51.0, 106.2, 110.8, 122.2, 122.6, 123.6, 123.9 (q, $^1J_{C\text{-}F}$ = 270.8 Hz), 125.0 (2C, q, $^3J_{C\text{-}F}$ = 3.8 Hz), 125.8 (2C), 126.4, 127.7, 128.9 (2C), 130.7 (2C), 131.1 (q, $^2J_{C\text{-}F}$ = 32.4 Hz), 135.0, 136.5, 136.6, 145.1, 165.4; IR (KBr) 1710, 1324, 1149, 1115, 1109 cm^{-1}; HRMS-EI: *m/z* $[M^+]$ calcd for $C_{24}H_{18}F_3NO_2$: 409.1290; found: 409.1289.

*Methyl 1-benzyl-2-(4-fluorophenyl)-1H-indole-3-carboxylate (**3g**):* 89% yield (105.6 mg) from **1g** (100 mg, 0.33 mmol), yellow soild, mp 106-107 °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.77 (3H, s), 5.17 (2H, s), 6.87-6.89 (2H, m), 7.06-7.10 (2H, m), 7.19-7.32 (8H, m), 8.26(1H, br-d, J = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 47.5, 50.8, 105.9, 110.7, 115.3 (2C, d, $^2J_{C\text{-}F}$ = 21.0 Hz), 122.1, 122.4, 123.3, 125.9 (2C), 126.6, 127.1 (d, $^4J_{C\text{-}F}$ = 3.9 Hz), 127.6, 128.4 (2C), 128.8 (2C), 132.1 (2C, d, $^3J_{C\text{-}F}$ =8.5 Hz), 136.4, 136.7, 145.9, 163.1 (d, $^1J_{C\text{-}F}$ =247.9 Hz) 165.4; IR (KBr) 1712, 1227, 1217, 1149, 1121 cm^{-1}; HRMS-EI: *m/z* $[M^+]$ calcd for $C_{23}H_{18}FNO_2$: 359.1322; found: 359.1320.

*Methyl 1-benzyl-2-(4-chlorophenyl)-1H-indole-3-carboxylate (**3h**):* 87% yield (101.4 mg) from **1h** (100 mg, 0.31 mmol), Colorless soild, mp 126-128°C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.78 (3H, s), 5.18 (2H, s), 6.87-6.89 (2H, m), 7.22-7.38 (10H, m), 8.26 (1H, br-d, J = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 47.5, 50.9, 105.9, 110.7, 122.1, 122.4, 123.3, 125.9 (2C), 126.6, 127.6, 128.4 (2C), 128.8 (2C), 129.6, 131.6 (2C), 135.3, 136.5, 136.7, 145.6, 165.4; IR (KBr) 1709, 1401, 1230, 1149 cm^{-1}; HRMS-EI: *m/z* $[M^+]$ calcd for $C_{23}H_{18}NO_2Cl$: 375.1026; found: 375.1025.

*Methyl 1-benzyl-2-(4-bromophenyl)-1H-indole-3-carboxylate (**3i**)*[13a]*:* 83% yield (97.7mg) from **1i** (100 mg, 0.28 mmol).

*Methyl 1-benzyl-2-(p-tolyl)-1H-indole-3-carboxylate (**3j**)*[13a]*:* 90% yield (108.5 mg) from **1j** (100 mg, 0.34 mmol).

*Methyl 1-benzyl-2-(4-(tert-butyl)phenyl)-1H-indole-3-carboxylate (**3k**):* 84% yield (96.8 mg) from **1k** (100 mg, 0.29 mmol), yellow soild, mp 118-120 °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.35 (9H, s), 3.80 (3H, s), 5.20 (2H, s), 6.92-6.94 (2H, m), 7.19-7.31 (8H, m), 7.41-7.44 (2H, m), 8.24 (1H, br-d, J = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.3 (3C), 34.8, 47.6, 50.8, 105.4, 110.8, 122.0, 122.2, 122.9, 125.1 (2C), 126.1 (2C), 126.8, 127.4, 128.0, 128.7 (2C), 129.8 (2C), 136.3, 137.0, 147.6, 152.0, 165.7; IR (KBr) 2963, 1702, 1687, 1460, 1164, 1149 cm^{-1}; HRMS-EI: *m/z* $[M^+]$ calcd for $C_{27}H_{27}NO_2$: 397.2042; found: 397.2041.

*Methyl 1-benzyl-5-methyl-2-phenyl-1H-indole-3-carboxylate (**3m**)*[13a]*:* 85% yield (102.7 mg) from **1m** (100 mg, 0.34 mmol).

*Methyl 1-benzyl-5,7-dimethyl-2-phenyl-1H-indole-3-carboxylate (**3n**):* 78% yield (92.4 mg) from **1n** (100 mg, 0.32 mmol), yellow soild, mp 127-130 °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.42 (3H, br-s), 2.45 (3H, s), 3.71 (3H, s), 5.34 (2H, s), 6.72-6.74 (2H, m), 6.81 (1H, s), 7.19-7.26 (5H, m), 7.32-7.39 (3H, m), 7.99 (1H, br-s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.6, 21.3, 49.1, 50.7, 105.6, 119.6, 121.0, 124.9 (2C), 127.1, 127.9, 127.9 (2C), 128.1, 128.8 (2C), 128.8, 130.0 (2C), 131.7, 131.8, 133.5, 139.1, 147.9, 165.7; IR (KBr) 1699, 1542, 1398, 1146, 1108 cm^{-1}; HRMS-EI: *m/z* $[M^+]$ calcd for $C_{25}H_{23}NO_2$: 369.1729; found: 369.1729.

*Methyl 1-benzyl-1H-indole-3-carboxylate (**3s**)* [13b]*:* 80% yield (102.2 mg) from **1s** (100 mg, 0.48 mmol).

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A simple change of ligand and solvent allows controlled, effective switching between cyclization-carbonylation and cyclization-carbonylation-cyclization-coupling (CCC-coupling) reactions.