JOC The Journal of Organic Chemistry

Article

pubs.acs.org/joc

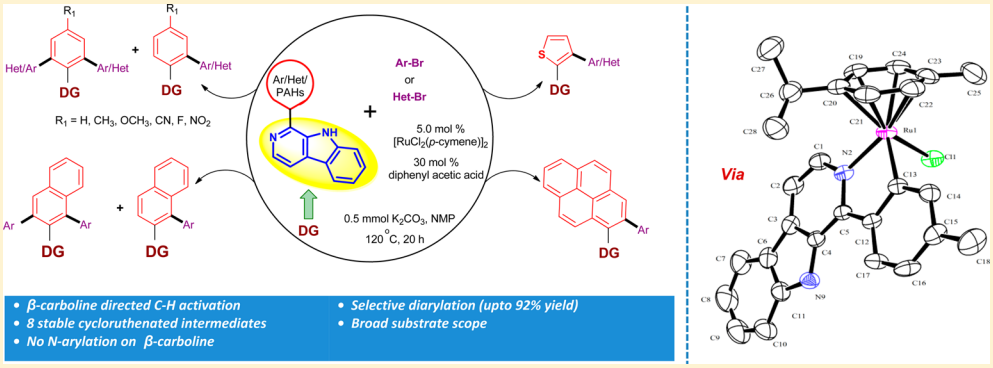
Ru(II)-Catalyzed β-Carboline Directed C−H Arylation and Isolation of Its Cycloruthenated Intermediates

Subramani Rajkumar,[†] Shanmugam Karthik,[†] and Thirumanavelan Gandhi*[,†,‡]

[†]Materials Chemistry Division, School of Advanced Sciences, VIT University, Vellore 632014, Tamil Nadu, India

[‡]Centre for Nanomaterials, VIT University, Vellore 632014, Tamil Nadu, India

Supporting Information



ABSTRACT: A Ru(II)-catalyzed C−H arylation approach has been developed utilizing β-carboline alkaloids as the directing group. Selective formations of diarylated products from moderate to excellent yields were accomplished. Broad substrate scope with excellent functional group tolerance for C1-phenyl/thienyl/PAHs-β-carbolines was demonstrated. X-ray crystal structure of cycloruthenated complex **2cr** and no arylation reaction with model substrate **13** strongly suggests that N2 is the directing group than N9 in C1-aryl-β-carbolines. Catalytic properties and stability of the cycloruthenated complexes have been explored. Library of biologically relevant new β-carboline derivatives and isolation of its cycloruthenated intermediates are the highlights of this work.

INTRODUCTION

Over the last few decades, transition metal-catalyzed C−H bond functionalization has been recognized as one of the more promising alternatives of traditional cross-coupling reactions.[1] Apart from being an alternative, the advancement in the area of C−H functionalization has advanced the synthesis of complex natural products, agrochemicals, polymers, and pharmaceutical targets in terms of productivity and economic viability.[2] Various directing groups and different transition metals have been implemented targeting diverse functionalizations.[3] In this regard, arylation reactions are among the most acclaimed and well-studied approaches of C−C bond formation. Consequently, a protocol capable of employing a biologically important scaffold as directing group will enrich the design of complex molecules for both in vivo and in vitro processes.

The β-carboline alkaloid is a naturally occurring scaffold actively involved in biologically active molecules[4] such as antibacterial, antimalarial, anti-inflammatory, antitumor, and anti-HIV drugs (Figure 1).[5] The structural resemblance of β-carboline alkaloids (C1-aryl-β-carbolines) with 2-phenylpyridine revealed its importance as a potential directing group.

The enhanced biological activity[6] of the hetero(aryl)/alkenyl substituted β-carboline core at the C1 and/or C3 position motivated us to utilize such a scaffold in the generation of new

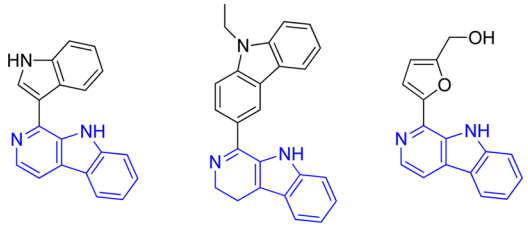


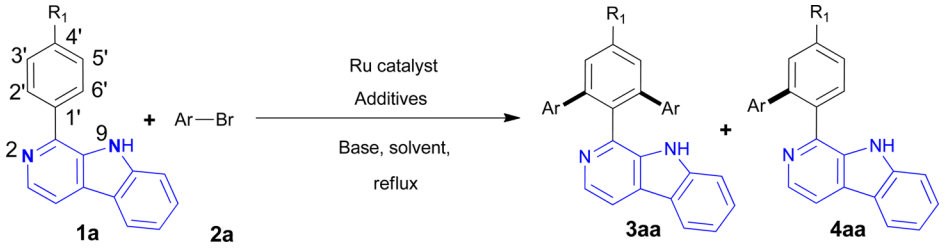
Figure 1. Representative natural products with C1 arylated β-carboline backbone.

bioactive target molecules. Notably, the presence of N9 along with N2 may also participate in C−H activation involving both 6-[7] and 5-membered cycloruthenated intermediates.[8] To facilitate the formation of the cycloruthenated intermediate and subsequent C−H functionalization, Ackermann,[9] Dixneuf[10] and other research groups[11] wisely utilized the carboxylates as a cocatalyst. Either bulky carboxylic acid or its ruthenium derivatives proved to be very efficient catalysts to promote C−H functionalization. Herein, simple and convenient β-carboline

Received: February 22, 2015
Published: April 10, 2015

DOI: 10.1021/acs.joc.5b00411
J. Org. Chem. 2015, 80, 5532−5545

Table 1. Optimization of Arylation Reactions[e]



entry	[Ru]	base	additives	solvent	conv. %	monoarylated **4aa**[d]	diarylated **3aa**[d]
1	–	K_2CO_3	KOAc	toluene	0	NR	NR
2	$[RuCl_2(p\text{-cymene})]_2$	Cs_2CO_3	KOAc	toluene	8	75	25
3	$[RuCl_2(p\text{-cymene})]_2$	K_2CO_3	KOAc	toluene	41	90	10
4	$[RuCl_2(p\text{-cymene})]_2$	K_2CO_3	KOAc	NMP	86	54	46
5	$[RuCl_2(p\text{-cymene})]_2$	K_2CO_3	HIPrCl[a]	NMP	90	21	79
6	$[RuCl_2(p\text{-cymene})]_2$	K_2CO_3	PPh_3	NMP	100	69	31
7	$[RuCl_2(p\text{-cymene})]_2$	K_2CO_3	PPh_3[b]	NMP	85	80	20
8	$[RuCl_2(p\text{-cymene})]_2$	K_2CO_3	$O{=}PPh_3$	NMP	100	53	47
9	$[RuCl_2(p\text{-cymene})]_2$	K_2CO_3	PCy_3	NMP	97	44	56
10	$[RuCl_2(p\text{-cymene})]_2$	K_2CO_3	$[(t\text{-Bu})_3PH]BF_4$	NMP	88	55	45
11	$[RuCl_2(p\text{-cymene})]_2$	K_2CO_3	$PhCO_2H$	NMP	100	35	65
12	$[RuCl_2(p\text{-cymene})]_2$	K_2CO_3	$t\text{-BuCO}_2H$	NMP	100	28	72
13	$[RuCl_2(p\text{-cymene})]_2$	K_2CO_3	$MesCO_2H$	NMP	100	25	75
14	$[RuCl_2(p\text{-cymene})]_2$	K_2CO_3	$(1\text{-Ad})CO_2H$	NMP	100	14 (10)[c]	86 (81)[c]
15	**$[RuCl_2(p\text{-cymene})]_2$**	**K_2CO_3**	**Ph_2HCCO_2H**	**NMP**	**100**	**11 (8)[c]**	**89 (85)[c]**
16	$[RuCl_2(benzene)]_2$	K_2CO_3	Ph_2HCCO_2H	NMP	100	10	90
17	$RuCl_3{\cdot}XH_2O$[12]	K_2CO_3	Ph_2HCCO_2H	NMP	85	11	88
18	$RuCl_3{\cdot}3H_2O$	K_2CO_3	Ph_2HCCO_2H	NMP	86	14	42
19	$Ru(DMSO)_4Cl_2$	K_2CO_3	Ph_2HCCO_2H	NMP	100	21	79
20	$[Ru(COD)Cl_2]_n$	K_2CO_3	Ph_2HCCO_2H	NMP	100	25	75
21	$RuCl_2(PPh_3)_3$	K_2CO_3	Ph_2HCCO_2H	NMP	100	30	70

[a]HIPrCl = *N*,*N*′-bis(2,6-diisopropyl phenyl)imidazolium chloride. [b]0.3 mmol of **2a** and 12 h. [c]Isolated yields. [d]Determined by GC; NR = No reaction. [e]Unless otherwise mentioned, all of the reactions were carried out with 0.2 mmol of **1a**, 0.5 mmol of **2a**, 5.0 mol % [Ru], 0.5 mmol of base, 30.0 mol % of additives, and 1.5 mL of solvent in a sealed tube at 120 °C for 20 h under N_2 atmosphere.

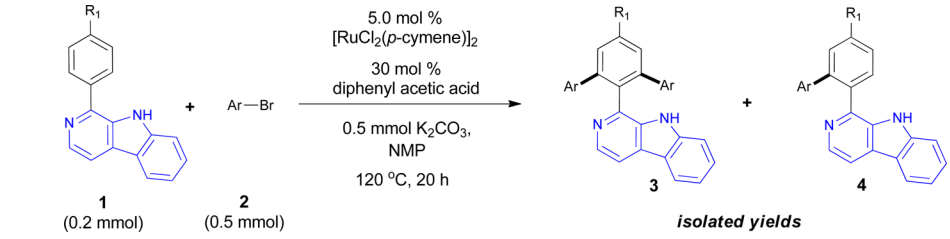
directed *ortho*-arylation of C1-(hetero)aryl/PAHs-*β*-carbolines by a ruthenium catalyst has been demonstrated. Notably, the isolation of a series of stable ruthenacycles under the standard condition revealed its role as an intermediate of this process.

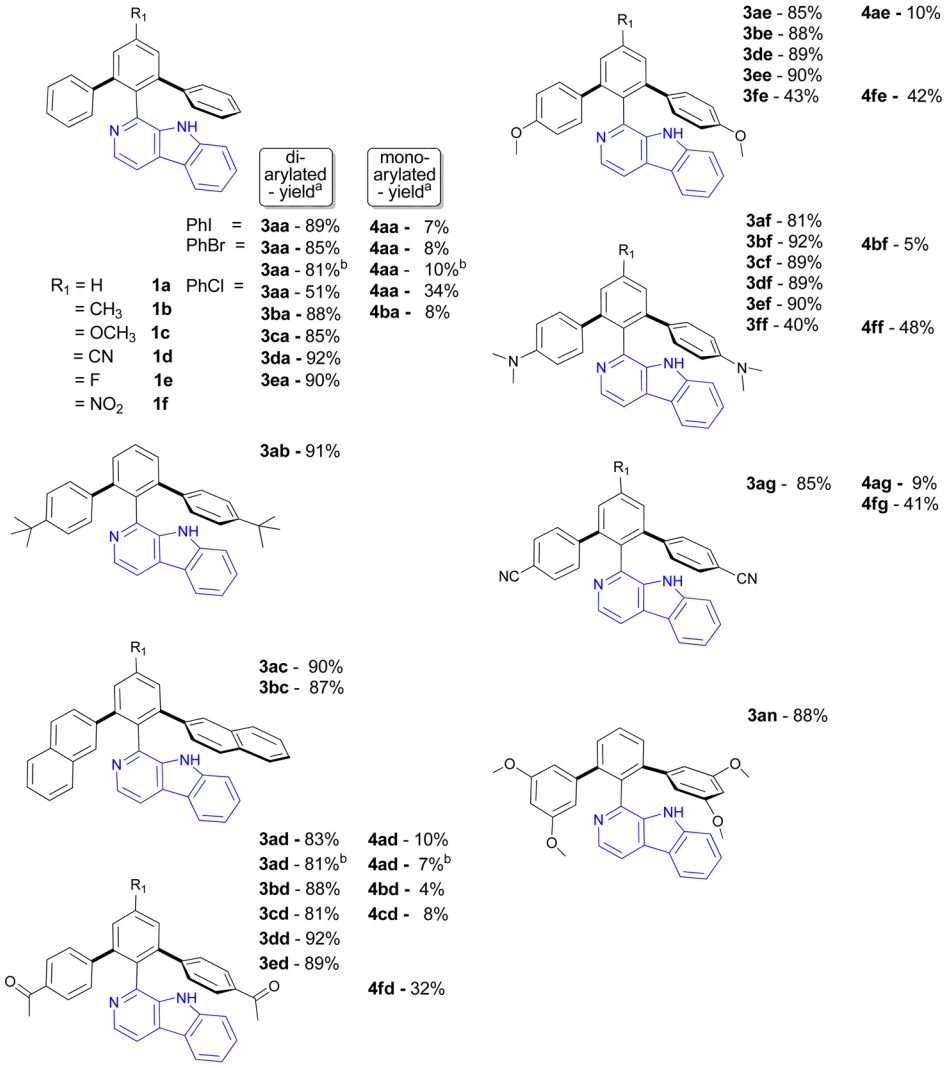
RESULTS AND DISCUSSION

Optimization of Ru(II)-Catalyzed Arylation. We began our catalytic arylation studies by combining 1-phenyl-*β*-carboline **1a** (0.2 mmol) with PhBr **2a** (0.5 mmol) in the presence of $[RuCl_2(p\text{-cymene})]_2$ (5 mol %), base (0.5 mmol) and additives (30 mol %) using solvents such as toluene, 1,4-dioxane, NMP and water. When the reaction was carried out in the absence of a ruthenium catalyst, predictably, there was no conversion of starting material (Table 1, entry 1). Pleasingly, the $[RuCl_2(p\text{-cymene})]_2$ (5 mol %) afforded the monoarylated and diarylated products, but in reduced conversion of 8% with an mono/di ratio of 75:25 (entry 2) in the presence of 0.5 mmol Cs_2CO_3, 30 mol % of KOAc using toluene as the solvent (20 h). To circumvent this issue, we chose K_2CO_3 as the base, resulting in an improved conversion 41% with an m/d ratio of 90:10 (entry 3). Solvents other than NMP resulted in reduced yields. Thus, toluene, 1,4-dioxane and H_2O were not considered. Among a set of additives such as acetate salts, *N*-heterocylic carbene, phosphines (/oxides) and carboxylic acids (entry 5−15), very promising results were obtained from phosphines and carboxylic acids, exhibiting some selectivity on the mono- and diarylation reaction. Remarkably, the reaction of **1a** and **2a** (0.5 mmol) in the presence of PPh_3 (30 mol %) and 0.5 mmol of K_2CO_3 resulted in complete conversion with a reduction in the m/d ratio of 69:31 (entry 6). Extending the concept of using phosphine-based additives, we attempted the reaction with $O{=}PPh_3$, PCy_3 and tri-*tert*-butylphosphonium tetrafluoroborate (TTBP·HBF_4). None of them exhibited improvement in the arylation selectivity (entry 8, 9 and 10). Interestingly, when we used 1,3-bis(2,6-diisopropylphenyl)imidazolinium chloride (HIPrCl) more diarylated product was observed with a m/d ratio of 21:79 (entry 5). Ackermann and Dixneuf have shown significant contribution in the field of Ru(II)-catalyzed arylation of (hetero)arene using carboxylic acids as additives, prompting us to evaluate them in our system.[9a,b,h,i,10a,b] Among a variety of carboxylic acids, which including pivalic acid, benzoic acid, mesitylene carboxylic acid, adamantane carboxylic acid and diphenyl acetic acid (entry 11−15), we found out that adamantane carboxylic acid and diphenyl acetic acid were very effective in furnishing the diarylated product with a m/d ratio of 14:86 and 11:89, respectively. From an economic and toxicity point of view, we have selected diphenyl acetic acid as the best choice. As far as a catalyst is concerned, $[RuCl_2(p\text{-cymene})]_2$ proved better than $RuCl_3{\cdot}xH_2O$, $RuCl_3{\cdot}3H_2O$, $[RuCl_2(DMSO)_4]$, $[RuCl_2(COD)]_n$ and $[RuCl_2(PPh_3)_3]$ (entry 17−21), as the former revealed improved yields. $[RuCl_2(p\text{-cymene})]_2$ and $[RuCl_2(benzene)]_2$ showed very similar results in the direct arylation studies. However,

DOI: 10.1021/acs.joc.5b00411
J. Org. Chem. 2015, 80, 5532−5545

Table 2. Ru(II)-Catalyzed Arylation Using Aryl Bromides[c]





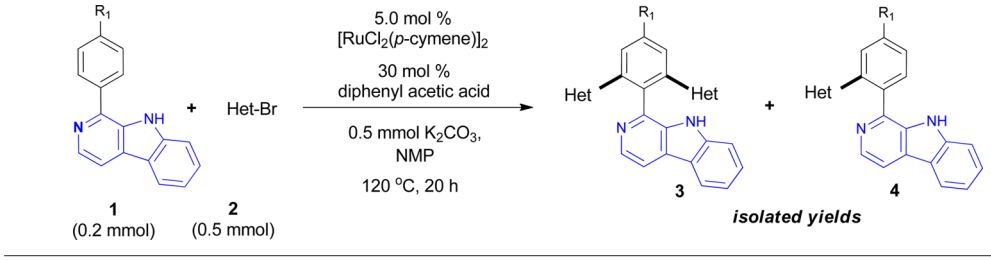
[a]Isolated yield. [b]Isolated yield (1-Ad)CO_2H (30 mol %). [c]**1** (0.2 mmol), **2** (0.5 mmol), $[RuCl_2(p\text{-cymene})]_2$ (5.0 mol %), K_2CO_3 (0.5 mmol), Ph_2CHCO_2H (30 mol %), NMP, 120 °C, 20 h.

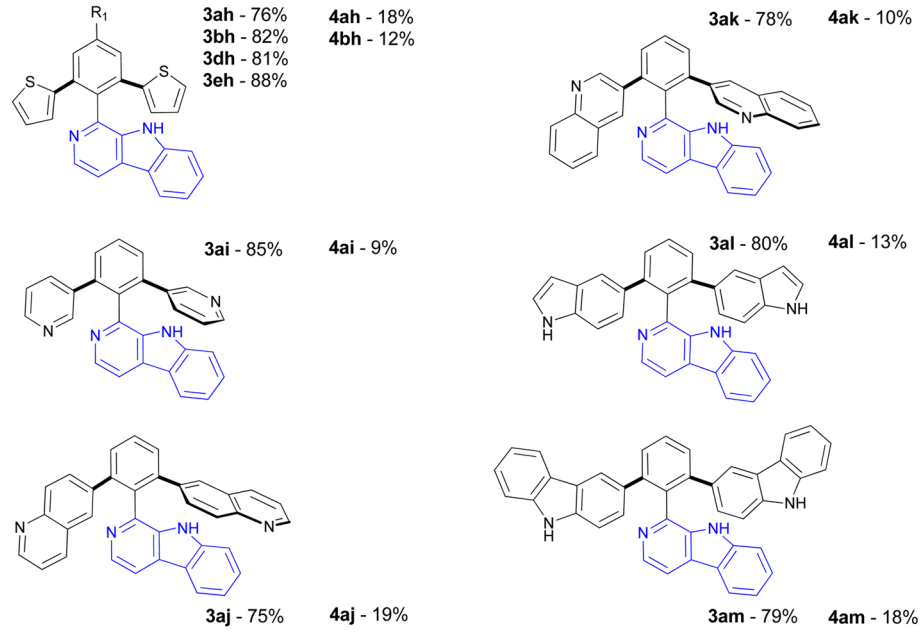
$[RuCl_2(p\text{-cymene})]_2$ is the least expensive (Table 1, entry 15). Consistently in all these reactions, no *N*-arylation of the indole ring in the β-carboline is observed.[13]

Scope of Ru(II)-Catalyzed Arylation of C1-Aryl-β-Carbolines Using Aryl Bromides and Heterocyclic Bromides. With the optimal conditions in hand, we have investigated the scope of the β-carboline-directed Ru-catalyzed *ortho*-arylation of 1-phenyl-β-carbolines using various aryl halides. *ortho*-Arylation using aryl iodides and aryl bromides showed promising results with good yields, whereas aryl chlorides produced a very low yield (Table 2). Substituents such as *t*-Bu- **2b**, MeCO- **2d**, MeO- 2e, Me_2N- **2f**, and -CN **2g** at the *para* position in aryl bromides were well tolerated under the reaction condition (Table 2). Interestingly, the various heterocyclic bromides such as thiophene **2h**, pyridine **2i**, isoquinoline **2j**, indole **2l** and carbazole **2m** show smooth arylation without poisoning the catalyst (Table 3). In general, diarylation proceeds smoothly irrespective of electron rich or electron poor aryl bromide partners employed. Next, we tested the reactivity by introducing the various functional groups such as methyl **1b**, methoxy **1c**, cyano **1d**, fluoro **1e**, and nitro **1f** at the C4′ position of the phenyl ring in C1-phenyl-β-carboline (Table 2 and 3). Functional groups such as -CN[14] and -NO_2[15] are well-known *ortho*-directing groups. However, these functional groups did not participate in the C—H activation process even with 5 equiv of aryl bromides.

DOI: 10.1021/acs.joc.5b00411
J. Org. Chem. 2015, 80, 5532−5545

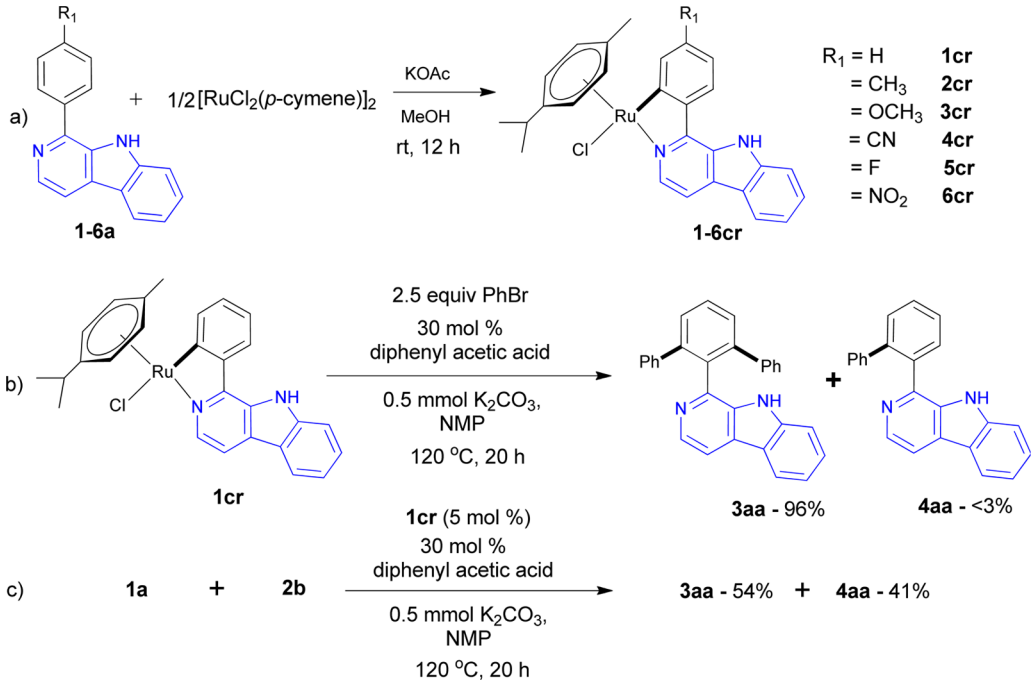
Table 3. Ru(II)-Catalyzed Arylation Using Hetroaryl Bromides[a,b]





[a]Isolated yield. [b]**1** (0.2 mmol), **2** (0.5 mmol), $[RuCl_2(p\text{-cymene})]_2$ (5.0 mol %), K_2CO_3 (0.5 mmol), Ph_2CHCO_2H (30 mol %), NMP, 120 °C, 20 h.

Scheme 1. Synthesis and Catalytic Property of Cycloruthenated C1-Phenyl-β-Carbolines



DOI: 10.1021/acs.joc.5b00411
J. Org. Chem. 2015, 80, 5532−5545

Synthesis and Reactivity of Cycloruthenated C1-Aryl-β-Carboline. The *ortho*-arylation reactions are expected to proceed via five or six-membered cyclometalation intermediates. To confirm this, various cyclometalation intermediates were synthesized by stoichiometric reaction of C1-aryl-β-carboline and $[RuCl_2(p\text{-cymene})]_2$ in the presence of KOAc (3 equiv) at room temperature (Scheme 1a). Cycloruthenation in C1-aryl-β-carbolines complexes was determined by ^{1}H NMR, i.e., by the disappearance of the *ortho* hydrogen of the 1-phenyl substituent. Additionally, the ^{13}C NMR showed significantly deshielded signals (ranging from δ = 176−196 ppm), which corroborated the existence of a Ru−C σ-bond in the structure. Eventually, the representative cycloruthenated complex **2cr** depicting N2 of the β-carboline coordinating to the ruthenium was unambiguously confirmed by single crystal X-ray diffraction study (Figure 2). To

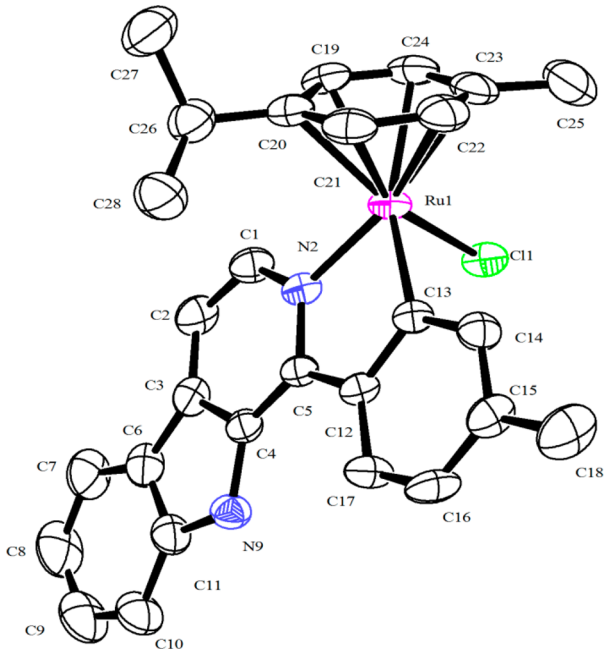


Figure 2. ORTEP diagram of Ru(II) complex **2cr** (50% probability ellipsoids). Hydrogen atoms and solvent molecules are omitted for clarity.

confirm the reactivity of the isolated cycloruthenated species, **1cr** was reacted with PhBr (2.5 equiv), which resulted in diarylated product in 96% yield (Scheme 1b). Such a reaction demonstrated that **1cr** is catalytically competent intermediate.[16] However, when **1cr** was used as a catalyst (5 mol %), it resulted in the decrease of selective arylation (Scheme 1c).

Cycloruthenated C1-aryl-β-carboline derivatives **1cr**−**8cr** were quite stable in solvents like methanol, dichloromethane and chloroform. However, in DMSO, they exhibit some reactivity, which was followed by ^{1}H NMR (Figure 3). The chloride ion present in **1cr** is replaced by DMSO to form **9cr** (Figure 3(2)) and eventually to **10cr** (Figure 3(3)) with the expulsion of η^6-*p*-cymene ligand (Scheme 2). Surprisingly, in the entire cases cycloruthenated moiety stays intact. Downfield peaks at δ 12.17 (◆), δ 11.88 (▲) and 11.75 ppm (▼) in Figure 3(2) corresponds to cycloruthenated β-carboline NH moiety of **9cr**, **10cr** and **1cr**, respectively. In ^{13}C NMR, cycloruthenated carbon (i.e., Ru−C) for **1cr** and **10cr** appears at δ 183.27 and δ 177.35 ppm, respectively. Presence of mixture of **1cr**, **9cr** and **10cr** was observed clearly on seventh day (Figure 3(2)), and subsequently on 14th day **1cr** and **9cr** was transformed to **10cr** (Figure 3(3)). Aromatic C−H's and η^6−*p*-cymene C−H's in **9cr** (◆) exhibited downfield shift compared to **1cr** (▼). Free *p*-cymene (★) expelled in the reaction were identified and matched with the authentic sample, and compound **10cr** was isolated and characterized by ^{1}H NMR, ^{13}C NMR and mass spectrometry.

Role of N2 and N9 in C1-Aryl-β-Carbolines As a Directing Group. In order to understand the role of N2 or N9 as a directing group in C1-aryl-β-carbolines, we have chosen a model substrate **13** (1-phenyl-9*H*-carbazole),[17] which is devoid of N2. Suprisingly, **13** remains unreactive in the arylation conditions, even when aryl bromide were taken in large excess (5 equiv) (Scheme 3). Thus, this model study strongly suggests that N2 have greater role in arylation of C1-aryl-β-carbolines derivatives than N9. In addition, the cycloruthanted complex **2cr** also supports the role of N2 as directing group over N9.

Scope of Ru(II)-Catalyzed C1-Thienyl-β-Carboline Using Aryl Bromides and Heterocyclic Bromides. We examined C−H arylation of C1-thienyl-β-carboline **5** by reacting with various aryl bromides **2a**−**2i**. When **5** reacted with a stoichiometic amount of $[RuCl_2(p\text{-cymene})]_2$ at room temperature in the presence of KOAc, an isolable rollover cycloruthenated intermediate[18] **7cr** was generated, which was characterized by multinuclear NMR and mass spectrometry (Table 4). Catalytically, the *ortho* C−H bond in the 1-thienyl moiety of **5** was activated and functionalized to give various new C3-arylated C1-thienyl-β-carboline derivatives **6a**−**6i** in good yields (Table 4). To the best of our knowledge, there is no report in the literature on the C3-arylation of 2-(thiophen-2-yl)pyridine scaffolds using ruthenium as a catalyst.

Scope of Ru(II)-Catalyzed C1-PAHs-β-Carboline Using Aryl Bromides. Next, we utilized this protocol to activate and functionalize the *ortho* C−H of PAHs (polyaromatic hydrocarbons) in C1-PAHs-β-carbolines (Table 5). The 2-naphthyl starting material **7** reacted with **2a** and **2d** to yield monoarylated products **8a** and **8d** via cycloruthenated intermediate **8cr** (see Supporting Information). Likewise, **10** reacted with **2d** to give **11d**, but formation of **12d** was not detected due to steric and energetically unfavorable 6-membered cycloruthenated intermediate formation.

Plausible Mechanism for Ru(II)-Catalyzed Arylation. In accord with previous Ru(II)-catalyzed direct arylation reactions,[1g,10c,16] we propose the arylation pathway in Scheme 4. The sequential mechanism involve concerted-metalation deprotonation (CMD) **C**, cycloruthenated species **D** (crystallographically characterized), oxidative addition, i.e., Ru(IV) species **E** and reductive elimination to give the arylated product. Isolation of cycloruthenated complexes **1cr**−**8cr** further substantiated this pathway.

■ CONCLUSION

In summary, we have demonstrated the effective utility of β-carboline as a directing group in Ru(II)-catalyzed *ortho*-arylation reactions. This approach is applicable in arylating (hetero)aryl and polyaromatic hydrocarbons attached to the β-carboline scaffold. Role of N2/N9 in C1-aryl-β-carbolines as a directing group was understood from model substrate **13** and X-ray crystal structure **2cr**. Besides, catalytic and stability studies of the cycloruthenated complex **1cr** have been explored. A series of cycloruthenated β-carboline intermediates, and a library of new functionalized C1-hetero(aryl)/PAHs-β-carbolines, have been

DOI: 10.1021/acs.joc.5b00411
J. Org. Chem. 2015, 80, 5532−5545

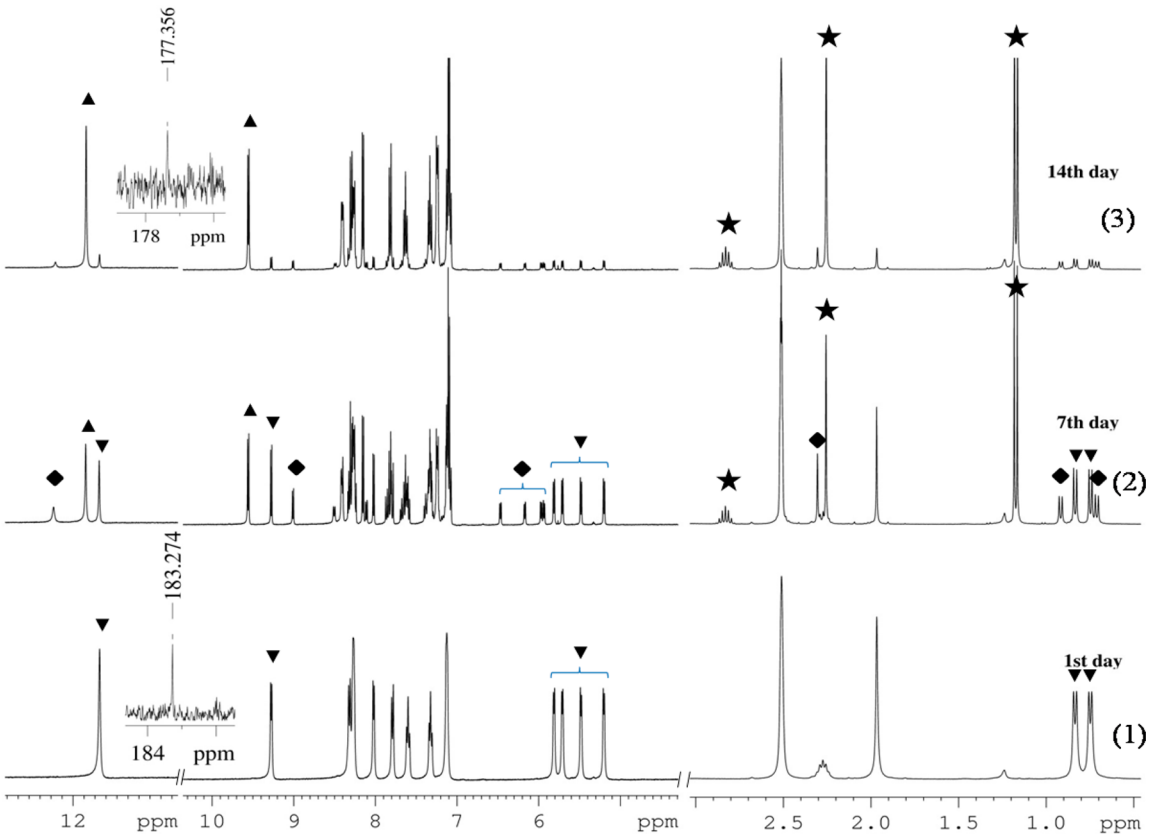
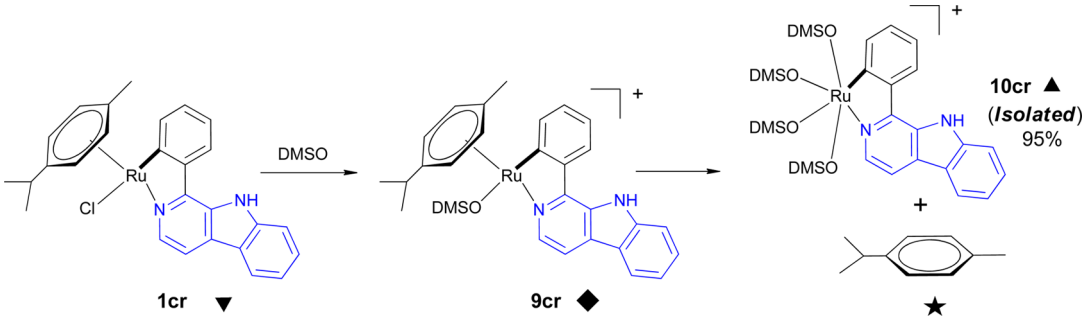
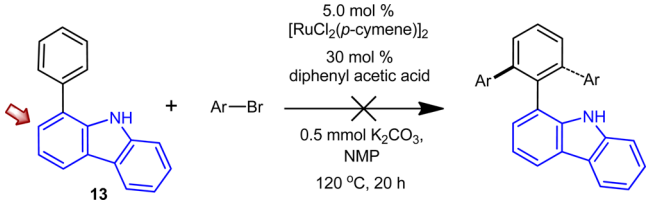


Figure 3. Stack plot of ^{1}H NMR spectra of the reaction of **1cr** with DMSO-d_6 with time. (1) **1cr** + DMSO-d_6 on 1st day; (2) **1cr** + DMSO-d_6 on 7th day; (3) **1cr** + DMSO-d_6 on 14th day. Insets were ^{13}C NMR chemical shift of cycloruthenated carbon on 1st (**1cr**) and 14th day (**10cr**). (▼) **1cr**, (◆) **9cr**, (▲) **10cr** and (★) free *p*-cymene.

Scheme 2. Reactivity of Cycloruthenated C1-Phenyl-*β*-Carboline Derivative 1cr in DMSO



Scheme 3. Tests of Arylation in the Absence of N2



synthesized, which is expected to possess photophysical properties and biological value.

EXPERIMENTAL SECTION

General Remarks. Unless otherwise mentioned, all the reactions were carried out under nitrogen purged screw cap reaction tubes. All solvents and reagents were of pure analytical grade. Various ruthenium catalysts were prepared from literature procedure.[19] The products were purified by column chromatography, silica gel (60−120 mesh or 200−420 mesh). A gradient elution using petroleum ether and ethyl acetate was performed based on precoated aluminumm TLC sheets (silica gel 60F 254).

Analytical Information. All isolated compounds were characterized by ^{1}H, ^{13}C and HRMS. Compound **2cr** was characterized by single crystal X-ray diffraction (Figure 1 and S1). Copies of the ^{1}H NMR, ^{13}C NMR can be found in the Supporting Information. All nuclear magnetic resonance spectra were recorded on 400 and 100 MHz NMR instrument for ^{1}H and ^{13}C NMR, respectively. All ^{1}H NMR spectra were reported in units ppm (parts per million), and were measured relative to the signals for residual chloroform (7.26 ppm) and DMSO (2.54 ppm) in the deuterated solvent. All ^{13}C NMR spectra were reported in ppm relative to deuterated chloroform (77.23 ppm) and DMSO (39.52 ppm). Coupling constants (*J*) are reported in Hz; splitting patterns are assigned s = singlet, d = doublet, t = triplet, q = quartet, quin = quintet; br = broad signal. GC MS and GC analyses were

DOI: 10.1021/acs.joc.5b00411
J. Org. Chem. 2015, 80, 5532−5545

Table 4. Ru-Catalyzed Arylation of C1-Thienyl-β-Carboline Using (Hetero)aryl Bromides

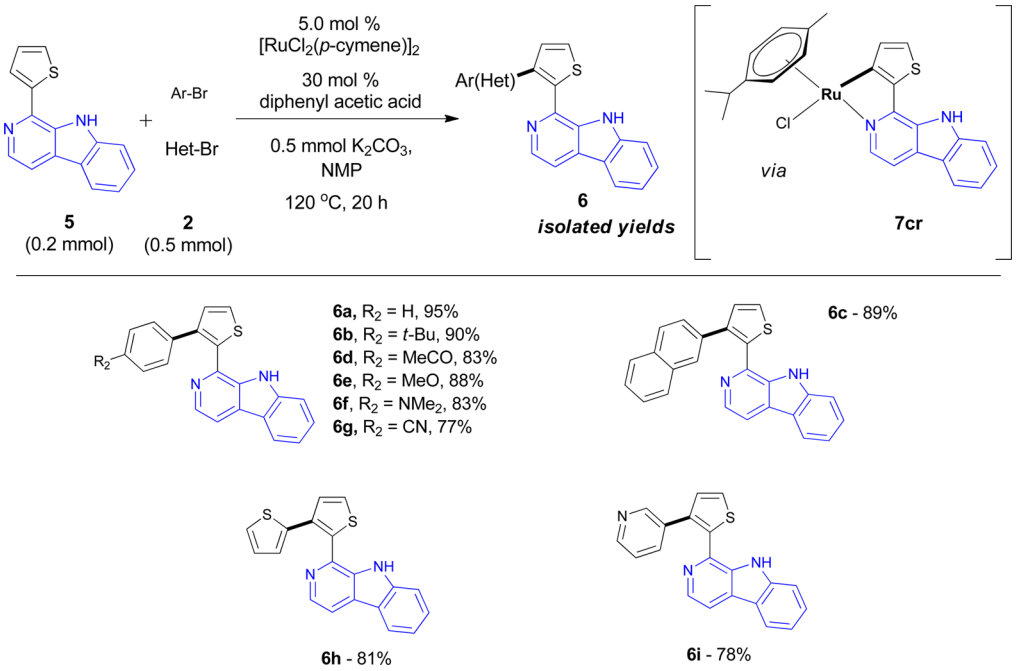
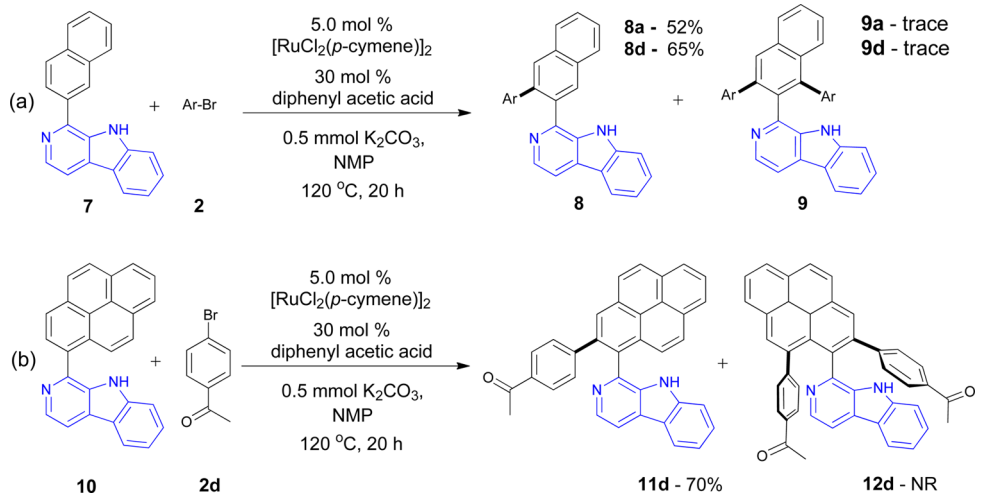


Table 5. Ru-Catalyzed Arylation of C1-PAHs-β-Carboline Using Aryl Bromides



performed with an FID detector; *n*-decane is the internal standard. High-resolution mass spectra (HRMS) were performed on TOF-Q analyzer.

General Synthetic Procedure for C1-(Hetero)aryl/PAHs-β-Carboline. All C1-(hetero)aryl/PAHs-β-carboline was synthesized by modifying the reported procedure.[20] Briefly a mixture of (hetero)aryl/PAHs aldehyde (1.1 mmol) and tryptamine (1.0 mmol) in anisole (10 mL) was heated to 120 °C over a period of 2 h, and then 5% Pd/C (0.5 mmol) was added and reflux at 140 °C for 24 h. The reaction mixture was filtered while hot, and the solvent was removed using rotary evaporation to give a reddish brown oil, which was dissolved in 1 mL of DCM, and petroleum ether was added, forming a yellow brown precipitate that is used for direct arylation without doing any further purification. Spectroscopic data of compounds **1a**−**1f**, **5**, and **7** matches well with the literature.[20b,21]

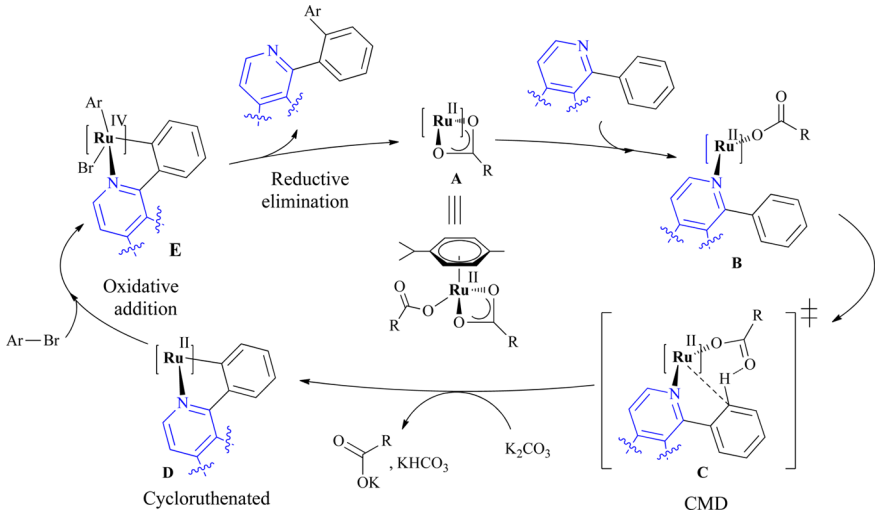
General Synthetic Procedure for Cycloruthenated Complexes (1cr−8cr). In an oven-dried, nitrogen gas flushed vial equipped with stirring bar, were placed C1-(hetero)aryl/PAHs-β-carboline (0.1 mmol), $[RuCl_2(p\text{-cymene})]_2$ (0.05 mmol, 30.6 mg), KOAc (0.3 mmol, 29.4 mg) and methanol (3−5 mL), and the mixture was stirred at ambient temperature for 12−20 h.[22] Yellow precipitate was formed, which was filtered and washed with diethyl ether to get pure solid cycloruthenated complex with good yield (80−90%).

Synthetic Procedure for 10cr. In an oven-dried, nitrogen gas flushed vial equipped with stirring bar, were placed **1cr** (52 mg, 0.1 mmol) and 0.5 mL of DMSO solvent, and the mixture was stirred at 65 °C for overnight. The resulting solution was evaporated, and the residue was purified by column chromatography using neutral alumina (DCM:MeOH = 95:5). The yellow fraction was collected and evaporated in a vacuum to get **10cr** Yield: 95%

General Synthetic Procedure for Direct Arylation. In an oven-dried, nitrogen gas flushed vial equipped with stirring bar, were placed C1-(hetero)aryl/PAHs-β-carboline (0.2 mmol), $[RuCl_2(p\text{-cymene})]_2$ (5 mol %, 0.01 mmol), diphenyl aceticacid (30 mol %, 0.06 mmol), anhydrous NMP (1.5 mL). The mixture stirred for 10 min at room temperature, followed by addition of K_2CO_3 (0.5 mmol) and aryl bromide (0.5 mmol). The reaction mixture was flushed with nitrogen, sealed with a Teflon-lined cap, and heated at 120 °C with stirring. After 20 h, the reaction mixture was diluted with water and extracted with ethyl acetate, the organic layer was washed with water and dried over

DOI: 10.1021/acs.joc.5b00411
J. Org. Chem. 2015, 80, 5532−5545

Scheme 4. Possible Mechanism for Ru-Catalyzed Arylation



Na_2SO_4, and solvent was evaporated under reduced pressure. The crude product was purified by column chromatography using petroleum ether and ethyl acetate as the solvent.

Cycloruthenated Complex ***1cr***. Yield: 43.6 mg, 85%; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.75 (s, 1H, NH), 9.28−9.26 (d, J = 8 Hz, 1H), 8.32−8.30 (d, J = 8 Hz, 1H), 8.27−8.26 (br, 2H), 8.02−8.01 (d, J = 4 Hz, 1H), 7.80−7.77 (d, J = 9.2 Hz, 1H), 7.61−7.58 (t, J = 6 Hz, 1H), 7.34−7.30 (t, J = 8 Hz, 1H), 7.12 (br, 2H), 5.82−5.80 (d, J = 8 Hz, 1H, p-cymene), 5.71−5.70 (d, J = 4 Hz, 1H, p-cymene), 5.48−5.47 (d, J = 4 Hz, 1H, p-cymene), 5.20−5.19 (d, J = 4 Hz, 1H, p-cymene), 2.27 (m, 1H, p-cymene-^{i}Pr−C−H), 1.96 (s, 3H, p-cymene-CH_3), 0.84−0.82 (d, J = 8 Hz, 3H, p-cymene-^{i}Pr-CH_3), 0.75−0.73 (d, J = 8 Hz, 3H, p-cymene-^{i}Pr-CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ 183.3 (C−Ru), 149.4, 145.1, 144.1, 141.4, 139.9, 131.0, 129.6, 128.7, 127.2, 125.2, 121.7, 121.6, 120.2, 120.1, 112.8, 112.7, 101.0, 98.2, 91.3, 89.5, 85.2, 81.9, 30.3, 22.2, 21.3, 18.4; HRMS (ESI) m/z calculated for $C_{27}H_{25}ClN_2NaRu$ [M + Na]$^+$ 537.0647, found 537.0647; m/z calculated for $C_{27}H_{25}N_2Ru$ [M − Cl]$^+$ 479.1061, found 479.1048.

Cycloruthenated Complex ***2cr***. Yield: 45.9 mg, 87%; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.65 (s, 1H, NH), 9.25−9.23 (d, J = 8 Hz, 1H), 8.32−8.31 (d, J = 4 Hz, 1H), 8.29−8.09 (m, 3H), 7.98−7.96 (d, J = 8 Hz, 1H), 7.77−7.75 (d, J = 8 Hz, 1H), 7.61−7.57 (t, J = 8 Hz, 1H), 7.33−7.30 (t, J = 8 Hz, 1H), 6.95−6.93 (d, J = 8 Hz, 1H), 5.82−5.80 (d, J = 8 Hz, 1H, p-cymene), 5.69−5.68 (d, J = 4 Hz, 1H, p-cymene), 5.49−5.47 (d, J = 8 Hz, 1H, p-cymene), 5.19−5.17 (d, J = 8 Hz, 1H, p-cymene), 2.42 (s, 3H), 2.29 (m, 1H, p-cym-^{i}Pr-CH), 1.97 (s, 3H, p-cymene-CH_3), 0.83−0.82 (d, J = 4 Hz, 3H, p-cymene-^{i}Pr-CH_3), 0.75−0.73 (d, J = 8 Hz, 3H, p-cymene-^{i}Pr-CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ 183.3 (C−Ru), 149.6, 145.0, 141.5, 141.3, 140.6, 136.3, 130.7, 129.4, 128.6, 124.9, 122.7, 121.5, 120.1, 112.6, 112.3, 101.0, 97.8, 91.4, 89.3, 85.5, 81.6, 48.6, 30.3, 22.2, 21.4, 18.4; HRMS (ESI) m/z calculated for $C_{28}H_{27}ClN_2NaRu$ [M + Na]$^+$ 551.0804, found 551.0801; m/z calculated for $C_{28}H_{27}N_2Ru$ [M − Cl]$^+$ 493.1218, found 493.1215.

Cycloruthenated Complex ***3cr***. Yield: 48.9 mg, 90%; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.65 (s, 1H, NH), 9.20−9.18 (d, J = 8 Hz, 1H), 8.29−8.27 (d, J = 8 Hz, 1H), 8.21−8.19 (d, J = 8 Hz, 1H), 7.92−7.91 (d, J = 4 Hz, 1H), 7.79−7.75 (m, 2H), 7.58−7.56 (t, J = 4 Hz, 1H), 7.32−7.29 (t, J = 6 Hz, 1H), 6.69−6.67 (d, J = 8 Hz, 1H), 5.79−5.78 (d, J = 4 Hz, 1H, p-cymene), 5.73−5.72 (d, J = 4 Hz, 1H, p-cymene), 5.48−5.47 (d, J = 4 Hz, 1H, p-cymene), 5.21−5.20 (d, J = 4 Hz, 1H), 3.91 (s, 3H), 2.3 (m, 1H, p-cymene-^{i}Pr-CH), 1.96 (s, 3H, p-cymene-CH_3), 0.86−0.84 (d, J = 8 Hz, 3H, p-cymene-^{i}Pr-CH_3), 0.76−0.74 (d, J = 8 Hz, 3H, p-cymene-^{i}Pr-CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ 185.6 (C−Ru), 157.7, 149.4, 145.0, 141.3, 137.2, 130.3, 129.1, 128.5, 126.1, 124.3, 121.5, 120.2, 120.1, 112.6, 111.7, 107.9, 101.0, 98.0, 90.9, 89.7, 85.3, 82.1, 54.8, 30.3, 22.3, 21.2, 18.3; HRMS (ESI) m/z calculated for $C_{28}H_{27}ClN_2NaORu$ [M + Na]$^+$ 567.0743, found 567.0702; m/z calculated for $C_{28}H_{27}N_2ORu$ [M − Cl]$^+$ 509.1167, found 509.1165.

Cycloruthenated Complex ***4cr***. Yield: 45.2 mg, 84%; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.92 (s, 1H, NH), 9.34−9.33 (d, J = 4 Hz, 1H), 8.61 (br, 1H), 8.39−8.35 (t, J = 8 Hz, 2H), 8.16−8.15 (d, J = 4 Hz, 1H), 7.79−7.77 (d, J = 8 Hz, 1H), 7.65−7.54 (m, 2H), 7.37−7.35 (d, J = 8 Hz, 1H), 5.93−5.92 (d, J = 4 Hz, p-cymene), 5.85−5.84 (d, J = 4 Hz, 1H, p-cymene), 5.61−5.60 (d, J = 4 Hz, 1H, p-cymene), 5.34−5.33 (d, J = 4 Hz, 1H), 2.2 (m, 1H, p-cymene-^{i}Pr-CH), 1.90 (s, 3H, p-cymene-CH_3), 0.83−0.81 (d, J = 8 Hz, 3H, p-cymene-^{i}Pr-CH_3), 0.75−0.74 (d, J = 4 Hz, 3H, p-cymene-^{i}Pr-CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ 183.4 (C−Ru), 148.7, 147.2, 145.5, 142.2, 141.7, 131.8, 130.4, 129.2, 125.3, 124.6, 121.8, 120.5, 120.1, 120.0, 114.4, 112.7, 108.9, 102.2, 99.0, 91.8, 89.5, 86.2, 82.2, 30.3, 22.1, 21.4, 18.4; HRMS (ESI) m/z calculated for $C_{28}H_{24}ClN_3NaRu$ [M + Na]$^+$ 562.0600, found 562.0698; m/z calculated for $C_{28}H_{24}N_3Ru$ [M − Cl]$^+$ 504.1014, found 504.1011.

Cycloruthenated Complex ***5cr***. Yield: 43.6 mg, 82%; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.72 (s, 1H, NH), 9.24−9.23 (d, J = 4 Hz, 1H), 8.32−8.26 (m, 2H), 8.02−8.00 (d, J = 8 Hz, 2H), 7.76−7.74 (d, J = 8 Hz, 1H), 7.61−7.57 (t, J = 8 Hz, 1H), 7.34−7.30 (t, J = 8 Hz, 1H), 6.92−6.88 (t, J = 8 Hz, 1H), 5.85−5.83 (d, J = 6 Hz, p-cymene), 5.76−5.75 (d, J = 4 Hz, 1H, p-cymene), 5.54−5.52 (d, J = 8 Hz, 1H, p-cymene), 5.26−5.25 (d, J = 4 Hz, 1H), 2.3 (m, 1H, p-cymene-^{i}Pr-CH), 1.97 (s, 3H, p-cymene-CH_3), 0.84−0.82 (d, J = 8 Hz, 3H, p-cymene-^{i}Pr-CH_3), 0.76−0.74 (d, J = 8 Hz, 3H, p-cymene-^{i}Pr-CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ 187.1 (C−Ru), 159.1, 148.4, 145.1, 141.5, 140.6, 130.7, 129.7, 128.8, 126.4, 126.3, 125.4, 125.2, 121.6, 120.3, 120.1, 112.8, 112.6, 108.6, 108.4, 101.6, 98.6, 91.4, 89.5, 85.8, 82.2, 30.7, 22.1, 21.3, 18.3; HRMS (ESI) m/z calculated for $C_{27}H_{24}ClFN_2NaRu$ [M + Na]$^+$ 555.0553, found 555.0551; m/z calculated for $C_{27}H_{24}FN_2Ru$ [M − Cl]$^+$ 497.0967, found 497.0964.

Cycloruthenated Complex ***6cr***. Yield: 44.7 mg, 80%; ^{1}H NMR (400 MHz, DMSO-d^6):δ 11.97 (s,1H, NH), 9.37−9.35 (d, J = 8 Hz, 1H), 8.96−8.95 (d, J = 4 Hz,1H), 8.45−8.43 (d, J = 8 Hz, 1H), 8.38−8.36 (d, J = 8 Hz, 1H), 8.20−8.19 (d, J = 4 Hz, 1H), 7.95−7.92 (m,1H), 7.80−7.78 (d, J = 8 Hz, 1H), 7.67−7.63 (t, J = 8 Hz, 1H), 7.39−7.35 (t, J = 8 Hz,1H), 5.93−5.92 (d, J = 4 Hz, 1H, p-cymene), 5.86−5.84 (d, J = 8 Hz, 1H, p-cymene), 5.63−5.62 (d, J = 4 Hz,1H, p-cymene), 5.37−5.35 (d, J = 8 Hz, 1H, p-cymene), 2.33 (m, 1H, p-cymene-^{i}Pr-CH), 2.01 (s, 3H, p-cymene-CH_3), 0.85−0.83 (d, J = 8 Hz, 3H, p-cymene-^{i}Pr-CH_3), 0.76−0.74 (d, J = 8 Hz, 3H, p-cymene-^{i}Pr-CH_3); ^{13}C NMR (100 MHz, DMSO- d^6):δ 184.7 (C−Ru), 150.7, 145.6, 144.9, 132.6, 130.6, 129.3, 124.7, 121.8, 120.6, 120.0, 117.0, 114.8, 112.7, 102.4, 99.4, 91.4, 90.0, 86.2, 82.5, 78.9, 30.4, 22.2, 21.2, 18.4; HRMS (ESI) m/z calculated for $C_{27}H_{24}ClN_3NaO_2Ru$ [M + Na]$^+$ 582.0498, found 582.0496; m/z calculated for $C_{27}H_{24}N_3O_2Ru$ [M − Cl]$^+$ 524.0912, found 524.0909.

Cycloruthenated Complex ***7cr***. Yield: 42.1 mg, 81%; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.24 (s, 1H, NH), 9.11−9.10 (d, J = 4 Hz, 1H), 8.27−8.25 (d, J = 8 Hz, 1H), 7.85−7.81 (br, 4H), 7.58−7.54 (t, J = 8 Hz, 1H), 7.32−7.28 (t, J = 8 Hz, 1H), 5.86−5.85 (d, J = 4 Hz, 2H, p-

DOI: 10.1021/acs.joc.5b00411
J. Org. Chem. 2015, 80, 5532−5545

cymene), 5.55−5.54 (d, J = 4 Hz, 1H, p-cymene), 5.32−5.30 (d, J = 8 Hz, 1H, p-cymene), 2.35 (m, 1H, p-cymene-^{i}Pr-CH), 1.97 (s, 3H, p-cymene-CH_3), 0.88−0.87 (d, J = 4 Hz, 3H, p-cymene- ^{i}Pr-CH_3), 0.78−0.76 (d, J = 8 Hz, 3H, p-cymene- ^{i}Pr-CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ 183.8 (C−Ru), 145.9, 144.8, 141.4, 137.2, 132.2, 128.9, 128.6, 128.4, 127.3, 121.6, 120.7, 120.1, 115.6, 113.1, 110.5, 100.6, 99.0, 89.7, 87.6, 85.5, 81.0, 30.4, 22.3, 21.4, 18.4; HRMS (ESI) m/z calculated for $C_{25}H_{23}ClN_2NaRuS$ $[M + Na]^+$ 543.0212, found 543.0211; m/z calculated for $C_{25}H_{23}N_2RuS$ $[M - Cl]^+$ 485.0625, found 485.0620.

Cycloruthenated Complex ***8cr***. Yield: 45.1 mg, 80%; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.94 (s,1H, NH), 9.37−9.36 (d, J = 4 Hz, 1H), 8.80 (s, 1H), 8.63 (s, 1H), 8.38−8.36 (d, J = 8 Hz, 1H), 8.13−8.12 (d, J = 4 Hz, 1H), 8.05−8.03 (d, J = 8 Hz, 1H), 7.86−7.80 (dd, J = 8.2 Hz, 2H), 7.68- 7.64 (t, J = 8 Hz, 1H), 7.51−7.48 (t, J = 6 Hz, 1H), 7.39 (q, J = 8 Hz, 2H), 5.90−5.89 (d, J = 4 Hz, 1H, p-cymene), 5.80−5.78 (d, J = 8 Hz, 1H p-cymene), 5.51−5.49 (d, J = 8 Hz, 1H p-cymene), 5.24−5.23 (d, J = 4 Hz, 1H), 2.30 (m, 1H, p-cymene- ^{i}Pr-CH), 2.02 (s, 3H, p-cymene-CH_3), 0.85−0.83 (d, J = 8 Hz, 3H, p-cymene- ^{i}Pr-CH_3), 0.73−0.71 (d, J = 8 Hz, 3H, p-cymene- ^{i}Pr-CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ 176.5 (C−Ru), 148.5, 145.5, 144.6, 141.6, 136.3, 133.3, 131.3, 130.3, 129.0, 128.3, 126.2, 125.5, 123.7, 123.1, 121.8, 120.4, 120.2, 113.7, 112.6, 101.6, 98.1, 91.7, 89.9, 85.0, 81.5, 48.6, 30.3, 22.2, 21.3, 18.4; HRMS (ESI) m/z calculated for $C_{31}H_{27}ClN_2NaRu$ $[M + Na]^+$ 587.0804, found 587.0800; m/z calculated for $C_{31}H_{27}N_2Ru$ $[M - Cl]^+$ 529.1218, found 529.1215.

Cycloruthenated Complex ***10cr***. Yield: 55.9 mg, 95%; ^{1}H NMR (400 MHz,DMSO-d_6) δ 11.82 (s, 1H, NH), 9.56−9.55 (d, J = 4 Hz, 1H), 8.37−8.28 (m, 2H), 8.15−8.14 (d, J = 4 Hz, 1H), 7.81−7.79 (d, J = 8 Hz, 1H), 7.65−7.61 (t, J = 8 Hz,1H), 7.35−731 (t, J = 8 Hz,1H), 7.24 (br, singlet, 2H), 2.51 (s, 6H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 177.3 (C−Ru), 149.5, 146.9, 141.9, 141.6, 140.5, 131.0, 130.7, 129.1, 127.6, 125.9, 121.9, 121.7, 120.3, 120.1, 112.8, 112.7, 47.6; HRMS (ESI) m/z calculated for $C_{25}H_{35}N_2NaO_4S_4Ru$ $[M + Na]^+$ 680.0421 found 680.0429.

1-([1,1′:3′,1″-Terphenyl]-2′-yl)-9H-pyrido[3,4-b]indole ***3aa***. White solid, Yield: 67.3 mg, 85%; R_f (PE/EA = 20/1) 0.7; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (d, J = 5.2 Hz, 1H), 7.92 (d, J = 7.9 Hz, 1H), 7.60−7.55 (m, 3H), 7.50 (d, J = 8.2 Hz, 2H), 7.38 (t, J = 7.6 Hz, 1H), 7.21 (d, J = 8 Hz, 1H), 7.14 (t, J = 7.4 Hz, 1H), 7.02−7.00 (m, 4H), 6.93−6.92 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.7, 142.2, 140.9, 140.0, 138.7, 136.9, 135.1, 129.8, 129.1, 128.9, 128.0, 127.7, 126.7, 121.7, 121.6, 119.8, 116.5, 113.3, 111.2; HRMS $[M + H]^+$ calculated for $C_{29}H_{20}N_2$ 397.1705, found 397.1697.

1-([1,1′-Biphenyl]-2-yl)-9H-pyrido[3,4-b]indole ***4aa***. White solid, Yield: 5.1 mg, 8%; R_f (PE/EA = 20/1) 0.7; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (d, J = 5.3 Hz, 1H), 7.98 (d, J = 8.0 Hz, 1H), 7.80 (d, J = 5.3 Hz, 1H), 7.68 (d, J = 7.0, 1.6 Hz, 1H), 7.68−7.47 (m, 4H), 7.37 (t, J = 8 Hz, 1H), 7.16−7.12 (m, 4H), 7.03−6.96 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.8, 140.5, 140.1, 139.4, 135.5, 133.7, 131.4, 130.4, 129.2, 128.9, 128.6, 128.3, 128.2, 128.0, 127.7, 127.2, 121.6, 119.9, 113.7, 111.1; HRMS $[M + H]^+$ calculated for $C_{23}H_{16}N_2$ 321.1392, found 321.1394.

1-(4,4″-Di-tert-butyl-[1,1′:3′,1″-terphenyl]-2′-yl)-9H-pyrido[3,4-b]indole ***3ab***. White solid, Yield: 92.5 mg, 91%; R_f (PE/EA = 20/1) 0.65; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, J = 5.6 Hz, 1H), 7.91 (d, J = 8 Hz, 1H), 7.61 (d, J = 5.2 Hz, 1H), 7.56−7.46 (m, 4H), 7.35 (t, J = 7.4 Hz, 1H), 7.17 (d, J = 8.4 Hz, 1H), 7.12 (t, J = 7.4 Hz, 1H), 6.92 (s, 8H), 1.01 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.5, 143.5, 142.6, 140.1, 138.6, 138.0, 135.3, 134.9, 129.5, 129.0, 128.6, 128.1, 127.8, 124.5, 121.6, 121.5, 119.6, 113.1, 111.0, 34.2, 31.1; HRMS $[M + H]^+$ calculated for $C_{37}H_{36}N_2$ 509.2957, found 509.2955.

1-(2,6-Di(naphthalen-2-yl)phenyl)-9H-pyrido[3,4-b]indole ***3ac***. White solid, Yield: 89.3 mg, 90%; R_f (PE/EA = 20/1) 0.71; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (d, J = 5.2 Hz, 1H), 7.83 (d, J = 8 Hz, 2H), 7.70 (s, 1H), 7.67 (br, 2H), 7.64−7.61 (m, 3H), 7.50−7.51 (m, 5H), 7.35 (d, J = 8.4 Hz, 2H), 7.29−7.24 (m, 5H), 7.17 (d, J = 8.2 Hz, 1H), 7.07−7.03 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.7, 139.9, 138.8, 138.4, 135.1, 133.0, 130.2, 129.2, 128.3, 128.0, 127.9, 127.4, 127.1, 127.0, 125.9, 125.7, 121.7, 121.6, 119.8, 113.4, 111.2; HRMS $[M + H]^+$ calculated for $C_{37}H_{24}N_2$ 497.2018, found 497.2020.

1,1′-(2′-(9H-Pyrido[3,4-b]indol-1-yl)-[1,1′:3,1″-terphenyl]-4,4″-diyl)diethanone ***3ad***. White solid, Yield: 79.7 mg, 83%; R_f (PE/EA = 20/1) 0.35; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (d, J = 5.6 Hz, 1H), 7.94 (d, J = 8 Hz, 1H), 7.64−7.61 (m, 3H), 7.55−7.51 (m, 6H), 7.40 (t, J = 8 Hz, 1H), 7.24 (d, J = 8 Hz, 1H), 7.17 (d, J = 8 Hz, 1H), 7.12 (m, 4H), 2.36 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.6, 145.5, 141.8, 140.0, 138.9, 135.3, 135.0, 131.0, 130.2, 129.4, 129.1, 128.4, 127.8, 121.8, 121.6, 120.2, 113.9, 111.3, 26.5; HRMS $[M + H]^+$ calculated for $C_{33}H_{24}N_2O_2$ 481.1916, found 481.1915.

1-(2′-(9H-Pyrido[3,4-b]indol-1-yl)-[1,1′-biphenyl]-4-yl)ethanone ***4ad***. White solid, Yield: 7.2 mg, 10%; R_f (PE/EA = 20/1) 0.4; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39 (d, J = 5.2 Hz, 1H), 8.01 (d, J = 8 Hz, 1H), 7.80 (d, J = 5.2 Hz, 1H), 7.75 (s, 1H), 7.66 (d, J = 6.8 Hz, 1H), 7.60 (d, J = 8 Hz, 1H), 7.51 (m, 3H), 7.40 (t, J = 7.6 Hz, 1H), 7.21−7.14 (m, 4H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.6, 145.6, 143.4, 140.0, 139.8, 139.4, 136.8, 135.4, 133.9, 131.0, 130.5, 129.3, 129.0, 128.9, 128.7, 128.4, 128.2, 121.7, 121.6, 120.1, 113.8, 111.2, 26.5; HRMS $[M + H]^+$ calculated for $C_{25}H_{18}N_2O$ 363.1497, found 363.1453.

1-(4,4″-Dimethoxy-[1,1′:3′,1″-terphenyl]-2′-yl)-9H-pyrido[3,4-b]indole ***3ae***. White solid, Yield: 77.5 mg, 85%; R_f (PE/EA = 20/1) 0.37; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (d, J = 4 Hz, 1H), 8.02 (d, J = 8 Hz, 1H), 7.77 (s, 1H), 7.72 (d, J = 4 Hz, 1H), 7.53 (d, J = 8 Hz, 2H), 7.48−7.44 (t, J = 8 Hz, 1H), 7.31−7.17 (m, 2H), 7.03 (d, J = 8 Hz, 4H), 6.57 (d, J = 8 Hz, 4H), 3.63 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.2, 143.5, 142.3, 140.1, 138.7, 136.6, 135.1, 134.5, 133.4, 131.4, 130.0, 129.4, 129.0, 128.0, 121.7, 121.7, 119.8, 113.3, 113.2, 111.3, 55.0; HRMS $[M + H]^+$ calculated for $C_{31}H_{24}N_2O_2$ 457.1916, found 457.1918.

1-(4′-Methoxy-[1,1′-biphenyl]-2-yl)-9H-pyrido[3,4-b]indole ***4ae***. White solid, Yield: 7.0 mg, 10%; R_f (PE/EA = 20/1) 0.41; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (d, J = 5.6 Hz, 1H), 8.10 (d, J = 8 Hz, 1H), 8.04 (s, 1H), 8.00 (d, J = 5.2 Hz, 1H), 7.75 (d, J = 7.6 Hz, 1H), 7.58 (d, J = 3.6 Hz, 2H), 7.53 (m, 2H), 7.29−7.26 (m, 1H), 7.16 (d, J = 8 Hz, 2H), 6.63 (d, J = 8.4 Hz, 2H), 3.61 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.0, 140.6, 133.3, 132.5, 131.6, 130.6, 130.3, 129.8, 127.9, 122.1, 120.7, 114.2, 114.0, 111.6, 55.1; HRMS $[M + H]^+$ calculated for $C_{24}H_{18}N_2O$ 351.1497, found 351.1460.

N^4,N^4,N^4″,N^4″-Tetramethyl-2′-(9H-pyrido[3,4-b]indol-1-yl)-[1,1′:3′,1″-terphenyl]-4,4″-diamine ***3af***. White solid, Yield: 78.1 mg, 81%; R_f (PE/EA = 20/1) 0.3; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (d, J = 5.6 Hz, 1H), 7.94 (d, J = 8 Hz, 1H), 7.65 (s, 1H), 7.61 (d, J = 4 Hz, 1H), 7.49−7.45 (m, 1H), 7.39−7.32 (m, 3H), 7.21 (d, J = 8 Hz, 1H), 7.13 (t, J = 5.8 Hz, 1H), 6.86 (d, J = 8 Hz, 4H), 6.29 (d, J = 8 Hz, 4H), 2.68 (s, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.0, 144.3, 142.7, 140.2, 138.8, 135.3, 134.2, 129.6, 129.3, 129.2, 128.9, 128.8, 128.0, 127.7, 121.9, 121.9, 121.6, 119.5, 113.0, 111.8, 111.4, 40.3; HRMS $[M + H]^+$ calculated for $C_{33}H_{30}N_4$ 483.2549, found 483.2546.

2′-(9H-Pyrido[3,4-b]indol-1-yl)-[1,1′:3′,1″-terphenyl]-4,4″-dicarbonitrile ***3ag***. White solid, Yield: 75.8 mg, 85%; R_f (PE/EA = 20/2) 0.63; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (d, J = 4 Hz, 1H), 8.04 (d, J = 8 Hz, 1H), 7.82 (d, J = 8.0 Hz, 1H), 7.75 (s, 1H), 7.69−7.67 (m, 1H), 7.67−7.41 (m, 4H), 7.45 (t, J = 6 Hz, 1H). 7.30−7.19 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.7, 142.2, 140.9, 140.0, 138.7, 136.9, 135.1, 129.8, 129.1, 128.9, 128.1, 127.7, 126.7, 121.7, 121, 6, 119.8, 116.5, 113.3, 111.2; HRMS $[M + H]^+$ calculated for $C_{31}H_{18}N_4$ 447.1610, found 447.1612.

2′-(9H-Pyrido[3,4-b]indol-1-yl)-[1,1′-biphenyl]-4-carbonitrile ***4ag***. White solid, Yield: 6.2 mg, 9%; R_f (PE/EA = 20/2) 0.66; ^{1}H NMR (400 MHz, CDCl3) δ 8.35 (d, J = 4 Hz, 1H), 8.04 (d, J = 8 Hz, 1H), 7.82 (d, J = 8.0 Hz, 1H), 7.75(s, 1H), 7.69−7.67 (m, 1H), 7.67−7.41 (m, 4H), 7.45(t, J = 6 Hz, 1H). 7.30−7.19(m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.5, 140.0, 139.3, 133.9, 131.8, 130.8, 130.6, 129.5, 129.2, 129.0, 128.7, 121.9, 121.6, 120.4, 118.7, 114.0, 111.2, 110.7; HRMS $[M + H]^+$ calculated for $C_{24}H_{15}N_3$ 346.1344, found 346.1299.

1-(3,3″,5,5″-Tetramethoxy-[1,1′:3′,1″-terphenyl]-2′-yl)-9H-pyrido-[3,4-b]indole ***3an***. White solid, Yield: 90.8 mg, 88%; R_f (PE/EA = 20/2) 0.57; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (d, J = 4 Hz, 1H), 7.93 (d, J = 8 Hz, 1H), 7.81 (s, 1H), 7.66 (d, J = 8 Hz, 1H), 7.53−7.48 (m, 2H), 7.37−7.33 (t, J = 8 Hz, 1H), 7.22−7.18 (t, J = 8 Hz, 2H), 7.15−7.11(t, J = 8 Hz, 1H), 6.21 (d, J = 3 Hz, 4H), 6.03 (s, 2H), 3.30 (s,12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.9, 143.5, 142.7, 142.6, 140.1, 138.5, 135.4, 134.4,

DOI: 10.1021/acs.joc.5b00411
J. Org. Chem. 2015, 80, 5532−5545

131.4, 130.0, 129.6, 129.2, 128.2, 121.7, 121.5, 120.0, 111.2, 107.1, 106.9, 99.8, 55.2, 55.0; HRMS $[M + H]^+$ calculated for $C_{33}H_{28}N_2O_4$ 517.2127, found 517.2124.

1-(2,6-Di(thiophen-2-yl)phenyl)-9H-pyrido[3,4-b]indole ***3ah***. Beige solid, Yield: 62.0 mg, 76%; R_f (PE/EA = 20/2) 0.64; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 (d, J = 4 Hz, 1H), 7.99 (d, J = 8 Hz, 1H), 7.82 (d, J = 8 Hz, 1H), 7.77 (s, 1H), 7.61−7.59 (d, J = 12 Hz, 2H), 7.51−7.49 (m, 1H), 7.38−7.34 (m, 1H), 7.17−7.12 (m, 3H), 6.90−6.88 (dd, J = 4 Hz, 2H), 6.65−6.53 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.2, 141.7, 140.1, 138.8, 135.6, 135.5, 133.8, 130.0, 129.3, 128.8, 128.3, 128.2, 127.4, 127.0, 126.8, 126.0, 126.0, 121.8, 121.7, 121.6, 120.0, 114.5, 111.5; HRMS $[M + H]^+$ calculated for $C_{25}H_{16}N_2S_2$ 409.0833, found 409.0830.

1-(2-(Thiophen-2-yl)phenyl)-9H-pyrido[3,4-b]indole ***4ah***. Beige solid, Yield: 11.7 mg, 18%; R_f (PE/EA = 20/2) 0.70; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (d, J = 5.2 Hz, 1H), 8.02 (d, J = 7.6 Hz, 1H), 7.87 (d, J = 5.2 Hz, 1H), 7.73 (s, 1H), 7.64−7.58 (m, 2H), 7.49−7.36 (m, 3H), 7.21−7.17 (m, 3H), 6.96 (d, J = 3.2 Hz, 1H), 6.62 (d, J = 4.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.6, 141.9, 140.2, 139.3, 136.5, 134.2, 133.3, 131.4, 130.2, 129.2, 128.8, 128.3, 128.2, 127.4, 126.6, 126.0, 121.7, 121.5, 120.0, 114.0, 111.3; HRMS $[M + H]^+$ calculated for $C_{21}H_{14}N_2S$ 327.0956, found 327.0903.

1-(2,6-Di(pyridin-3-yl)phenyl)-9H-pyrido[3,4-b]indole ***3ai***. Beige solid, Yield: 67.6 mg, 85%; R_f (PE/EA = 20/20) 0.45; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.17 (s, 1H), 8.25 (s, 2H), 8.17−8.14 (m, 3H), 8.08 (d, J = 8 Hz, 1H), 7.87 (d, J = 4 Hz, 1H), 7.82−7.79 (t, J = 6 Hz, 1H), 7.67 (d, J = 8 Hz, 2H), 7.45−7.41 (t, J = 8 Hz, 4H), 7.16−7.13 (t, J = 6 Hz, 1H), 7.06−7.03 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 148.9, 147.6, 141.9, 140.6, 139.0, 137.3, 136.1, 135.8, 135.0, 130.0, 129.2, 127.9, 127.2, 122.5, 121.6, 120.3, 119.1, 113.8, 111.9; HRMS $[M + H]^+$ calculated for $C_{27}H_{18}N_4$ 399.1610, found 399.1607.

1-(2-(Pyridin-3-yl)phenyl)-9H-pyrido[3,4-b]indole ***4ai***. Beige solid, Yield: 5.7 mg, 9%; R_f (PE/EA = 20/10) 0.55; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.10 (s, 1H), 8.30 (d, J = 8 Hz, 1H), 8.2 (s, 1H), 8.20−8.17 (m, 2H), 8.04 (d, J = 4 Hz, 1H), 7.70−7.64 (m, 4H), 7.48−7.43 (m, 3H), 7.21−7.18 (t, J = 6 Hz, 1H), 7.10−7.07 (m, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 149.0, 147.5, 143.2, 140.8, 137.7, 137.6, 137.1, 136.1, 135.8, 133.8, 130.6, 130.4, 129.0, 128.2, 128.0, 128.0, 122.7, 121.6, 120.5, 119.2, 113.8, 112.0; HRMS $[M + H]^+$ calculated for $C_{22}H_{15}N_3$ 322.1344, found 322.1342.

1-(2,6-Di(quinolin-6-yl)phenyl)-9H-pyrido[3,4-b]indole ***3aj***. White solid, Yield: 74.7 mg, 75%; R_f (PE/EA = 20/20) 0.44; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.19 (s, 1H), 8.74 (, J = 4 Hz, 1H), 8.10 (s, 1H), 8.09 (d, J = 4 Hz, 2H), 7.98−7.74 (m, 8H), 7.58 (d, J = 8 Hz, 2H), 7.41−7.36 (m, 6H), 7.08−7.05 (m, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 150.3, 146.2, 141.6, 140.5, 139.0, 135.8, 135.1, 130.5, 130.0, 129.0, 127.9, 127.8, 127.5, 127.1, 121.5, 120.2, 119.0, 113.6, 111.8; HRMS $[M + H]^+$ calculated for $C_{35}H_{22}N_4$ 499.1923, found 499.1926.

1-(2-(Quinolin-6-yl)phenyl)-9H-pyrido[3,4-b]indole ***4aj***. White solid, Yield: 14.1 mg, 19%; R_f (PE/EA = 20/10) 0.60; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.66 (dd, J = 4.2 Hz, 1H), 8.35 (d, J = 5.3 Hz, 1H), 8.03 (s, 1 H), 7.95 (d, J = 8 Hz, 1H), 7.85 (dd, J = 8 Hz, 1H), 7.76 (d, J = 5.2 Hz, 1H), 7.66 (dd, J = 7.6 Hz, 2H), 7.65 (s, 2H), 7.63−7.60 (m, 1H), 7.58−7.36 (m, 2H), 7.35−7.20 (m, 2H),7.29−7.03 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.3, 147.1, 143.6, 140.1, 140.0, 139.3, 139.1, 136.9, 136.0, 134.0, 130.9, 130.6, 129.3, 129.0, 128.0, 127.5, 121.7, 121.5, 121.2, 120.0, 113.8, 111.2; HRMS $[M + H]^+$ calculated for $C_{26}H_{17}N_3$ 372.1501, found 372.1488.

1-(2,6-Di(quinolin-3-yl)phenyl)-9H-pyrido[3,4-b]indol ***3ak***. White solid, Yield: 77.7 mg, 78%; R_f (PE/EA = 20/20) 0.52; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.30 (s, 1H), 8.50 (s, 2H), 8.19−8.10 (br, 3H), 8.00 (br, 1H), 8.01 (d, J = 5.3 Hz, 1H), 8.00−7.87 (m, 7H), 7.63 (m, 2H), 7.51 (m, 2H), 7.41 (s, 2H), 7.11 (br, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 155.5, 151.1, 147.1, 145.9, 144.2, 142.7, 141.3, 140.4, 140.3, 138.9, 135.9, 134.6, 133.6, 133.2, 132.6, 132.0, 132.0, 126.9, 125.5, 124.4, 119.2, 117.1; HRMS $[M + H]^+$ calculated for $C_{35}H_{22}N_4$ 499.1844, found 499.1848.

1-(2-(Quinolin-3-yl)phenyl)-9H-pyrido[3,4-b]indole ***4ak***. White solid, Yield: 7.4 mg, 10%; R_f (PE/EA = 20/10) 0.65; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.20 (s, 1H), 8.43 (d, J = 2.2 Hz, 1H), 8.23 (d, J = 5.2 Hz, 1H), 8.21−8.05 (m, 2H), 8.01 (d, J = 5.3 Hz, 1H), 7.79−7.69 (m, 5H), 7.64 (s, 1H), 7.62 (d, J = 8 Hz, 1H), 7.51−7.48 (m, 1H), 7.44 (br, 2H), 7.19−7.15 (m, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 150.6, 145.8, 143.2, 140.8, 137.8, 137.5, 137.3, 134.7, 134.0, 133.8, 130.9, 130.6, 129.3, 129.1, 128.3, 128.0, 127.1, 126.6, 121.6, 120.5, 119.2, 113.8, 112.0; HRMS $[M + H]^+$ calculated for $C_{26}H_{17}N_3$ 372.1501, found 372.1481.

1-(2,6-Di(1H-indol-5-yl)phenyl)-9H-pyrido[3,4-b]indole ***3al***. White solid, Yield: 75.8 mg, 80%; R_f (PE/EA = 20/20) 0.35; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.93 (s, 1H), 10.86 (s, 2H), 8.11 (d, J = 4 Hz, 1H), 8.01 (d, J = 8 Hz, 1H), 7.72 (d, J = 4 Hz, 2H), 7.69−7.65 (m, 2H), 7.40−7.36 (m, 4H), 7.17 (t, J = 3 Hz, 2H), 7.09 (m, 1H), 6.96 (d, J = 8.4 Hz, 2H), 6.80 (dd, J = 8.4 Hz, 2H), 6.20 (s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 144.5, 143.6, 140.4, 136.8, 135.4, 135.2, 134.3, 132.1, 129.2, 128.0, 127.3, 126.9, 126.4, 125.2, 122.4, 121.3, 120.5, 120.4, 118.6, 112.9, 111.9, 109.9, 101.0; HRMS $[M + H]^+$ calculated for $C_{33}H_{22}N_4$ 475.1923, found 475.1925.

1-(2-(1H-Indol-5-yl)phenyl)-9H-pyrido[3,4-b]indole ***4al***. White solid, Yield: 9.3 mg, 13%; R_f (PE/EA = 20/10) 0.4; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (d, J = 5.2 Hz, 1H), 8.02 (d, J = 7.6 Hz, 2H), 7.87 (d, J = 5.2 Hz, 1H), 7.82−7.67 (m, 3H), 7.61 (s, 2H), 7.65−7.50 (m, 2H), 7.35 (t, J = 7.7 Hz, 1H), 7.21−6.96 (m, 4H), 6.46 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.5, 140.1, 139.4, 133.8, 132.8, 131.6, 130.8, 129.0, 128.6, 128.1, 127.9, 127.2, 124.7, 123.2, 121.4, 121.4, 120.5, 119.6, 113.5, 111.0, 110.9, 102.8; HRMS $[M + H]^+$ calculated for $C_{25}H_{17}N_3$ 360.1501, found 360.1457.

1-(2,6-Di(9H-carbazol-3-yl)phenyl)-9H-pyrido[3,4-b]indole ***3am***. White solid, Yield: 90.7 mg, 79%; R_f (PE/EA = 20/20) 0.45; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.07 (s, 1H), 11.03 (s, 2H), 8.10 (d, J = 4 Hz, 1H), 7.94−7.91 (m, 3H), 7.75 (d, J = 8 Hz, 3H), 7.67 (d, J = 4 Hz, 1H), 7.64 (d, J = 8 Hz, 2H), 7.41−7.27 (m, 6H), 7.12−7.03 (m, 7H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 144.3, 143.1, 140.4, 139.8, 138.1, 136.8, 135.7, 135.4, 131.6, 129.2, 128.3, 127.4, 126.6, 126.5, 125.3, 122.2, 121.6, 121.4, 120.5, 119.5, 118.7, 118.1, 118.8, 110.9, 109.6; HRMS $[M + H]^+$ calculated for $C_{41}H_{26}N_4$ 575.2236, found 575.2235.

1-(2-(9H-Carbazol-3-yl)phenyl)-9H-pyrido[3,4-b]indole ***4am***. White solid, Yield: 14.7 mg, 18%; R_f (PE/EA = 20/10) 0.5; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46 (d, J = 5.2 Hz, 1H), 8.05 (s, 1H), 7.97 (s, 1H), 7.89 (d, J = 8 Hz, 1H), 7.81 (d, J = 7.6 Hz, 1H), 7.76 (d, J = 5.2 Hz, 1H) 7.68−7.61 (m, 3H), 7.53 (t, J = 7.6 Hz, 1H), 7.43 (t, J = 7.5 Hz, 1H), 7.24−7.15 (m, 3H), 7.09 (m, 3H), 6.97 (d, J = 8.2 Hz, 1H), 6.85 (d, J = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.5, 141.3, 140.0, 139.8, 139.3, 138.6, 136.9, 133.8, 132.1, 131.5, 130.9, 129.2, 128.8, 128.0, 127.4, 126.7, 125.8, 123.5, 123.1, 121.5, 121.4, 120.2, 120.2, 119.7, 119.4, 113.6, 111.1, 110.6, 110.4; HRMS $[M + H]^+$ calculated for $C_{29}H_{19}N_3$ 410.1657, found 410.1640.

1-(5-Methyl-[1,1′-biphenyl]-2-yl)-9H-pyrido[3,4-b]indole ***3ba***. White solid, Yield: 72.1 mg, 88%; R_f (PE/EA = 20/1) 0.75; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 (d, J = 5.2 Hz, 1H), 7.97 (d, J = 8.0 Hz, 1H), 7.78 (d, J = 5.2 Hz, 1H), 8.44 (d, J = 7.7 Hz, 1H), 7.51 (s, 1H), 7.36−7.34 (m, 3H), 7.31 (d, J = 2.6 Hz, 1H), 7.17−7.11 (m, 5H), 7.01−6.92 (m, 5H), 2.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.9, 140.4, 140.1, 139.2, 139.1, 133.8, 131.3, 131.1, 128.8, 128.5, 128.3, 128.2, 127.2, 121.6, 121.4, 119.9, 113.5, 111.0, 21.4; HRMS $[M + H]^+$ calculated for $C_{30}H_{22}N_2$ 411.1861, found 411.1863.

1-(5-Methyl-[1,1′-biphenyl]-2-yl)-9H-pyrido[3,4-b]indole ***4ba***. White solid, Yield: 5.3 mg, 8%; R_f (PE/EA = 20/1) 0.8; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (d, J = 5.3 Hz, 1H), 7.97 (d, J = 7.6 Hz, 1H), 7.78 (d, J = 5.2 Hz, 1H), 7.57−7.55 (m, 2H), 7.36−7.27 (m, 3H), 7.16−7.10 (m, 4H), 7.02−6.93 (m, 3H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.9, 140.9, 140.4, 140.1, 139.1, 139.1, 133.8, 131.3, 131.1, 128.8, 128.5, 128.3, 128.2, 127.2, 121.6, 121.4, 119.9, 113.5, 111.0, 21.3; HRMS $[M + H]^+$ calculated for $C_{24}H_{18}N_2$:335.1548, found 335.1550.

1-(4-Methyl-2,6-di(naphthalen-2-yl)phenyl)-9H-pyrido[3,4-b]-indole ***3bc***. White solid, Yield: 88.7 mg, 87%; R_f (PE/EA = 20/1) 0.52; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (d, J = 4 Hz, 1H), 7.83 (d, J = 8 Hz, 1H), 7.70−7.49 (m, 9H), 7.43 (s, 2H), 7.34 (d, J = 8 Hz, 2H), 7.28−7.24 (m, 4H), 7.16 (d, J = 12 Hz, 1H), 7.06 (m, 3H), 2.52 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.6, 139.9, 139.0, 138.8, 138.6, 135.3, 133.0, 132.0, 131.0, 128.2, 128.0, 127.4, 127.0, 125.8, 125.7, 121.7, 119.7, 113.3,

DOI: 10.1021/acs.joc.5b00411
J. Org. Chem. 2015, 80, 5532−5545

111.2, 21.4; HRMS $[M + H]^+$ calculated for $C_{38}H_{26}N_2$ 511.2174, found 511.2170.

1,1′-(5′-Methyl-2′-(9H-pyrido[3,4-b]indol-1-yl)-[1,1′:3′,1″-terphenyl]-4,4″-diyl)diethanone ***3bd***. White solid, Yield: 86.9 mg, 88%; R_f (PE/EA = 20/2) 0.44; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, J = 5.3 Hz, 1H), 7.93 (d, J = 7.9 Hz, 1H), 7.62 (d, J = 5.4 Hz, 2H), 7.54 (d, J = 8.4 Hz, 4H), 7.39−7.35 (m, 1H), 7.33 (s, 2H), 7.21 (d, J = 8.2 Hz, 1H), 7.14−7.09 (m, 4H), 2.49 (s, 3H), 2.35 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.7, 145.7, 141.7, 139.9, 139.3, 138.9, 135.3, 135.1, 130.9, 129.1, 128.4, 127.8, 121.8, 121.6, 120.1, 113.7, 111.3, 26.5, 21.3; HRMS $[M + H]^+$ calculated for $C_{34}H_{26}N_2O_2$ 495.2073, found 495.2086.

1-(5′-Methyl-2′-(9H-pyrido[3,4-b]indol-1-yl)-[1,1′-biphenyl]-4-yl)-ethanone ***4bd***. White solid, Yield: 3.0 mg, 4%; R_f (PE/EA = 20/2) 0.48; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (d, J = 5.2 Hz, 1H), 8.01 (d, J = 8 Hz, 1H), 7.80 (d, J = 5.2 Hz, 1H), 7.75 (s, 1H), 7.66 (d, J = 6.8 Hz, 1H), 7.60 (d, J = 8 Hz, 1H), 7.51 (m, 3H), 7.40 (t, J = 7.6 Hz, 1H), 7.21−7.14 (m, 4H), 2.45 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.7, 145.8, 143.5, 140.0, 139.6, 139.4, 139.2, 135.4, 133.9, 131.2, 131.0, 129.4, 128.9, 128.8, 128.3, 128.2, 121.7, 121.6, 120.1, 113.7, 111.2, 26.5, 21.4; HRMS $[M + H]^+$ calculated for $C_{26}H_{20}N_2O$ 377.1654, found 377.1657.

1-(4,4″-Dimethoxy-5′-methyl-[1,1′:3′,1″-terphenyl]-2′-yl)-9H-pyrido[3,4-b]indole ***3be***. White solid, Yield: 82.7 mg, 88%; R_f (PE/EA = 20/2) 0.5; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, J = 4 Hz, 1H), 7.93 (d, J = 8 Hz, 1H), 7.61 (s, 2H), 7.60−7.58 (d, J = 8 Hz, 1H), 7.37−7.33 (m, 2H), 7.23−7.14 (m, 2H), 6.92−6.89 (m, 4H), 6.46−6.43 (m, 4H), 3.53 (s, 6H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.2, 143.7, 142.2, 140.0, 138.7, 138.6, 135.2, 133.5, 131.7, 130.2, 130.0, 128.0, 127.9, 121.8, 121.7, 119.7, 113.1, 111.3, 55.0, 21.4; HRMS $[M + H]^+$ calculated for $C_{32}H_{26}N_2O_2$ 471.2073, found 471.2075.

N^4,N^4,$N^{4″}$,$N^{4″}$,5′-Pentamethyl-2′-(9H-pyrido[3,4-b]indol-1-yl)-[1,1′:3′,1″-terphenyl]-4,4″-diamine ***3bf***. White solid, Yield: 91.3 mg, 92%; R_f (PE/EA = 20/2) 0.4; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (d, J = 5.3 Hz, 1H), 7.94 (d, J = 7.8 Hz, 1H), 7.64 (s, 1H), 7.60 (d, J = 5.2 Hz, 1H), 7.36−7.32 (m, 3H), 7.18 (s, 1H), 7.11 (t, J = 14.9, 7.7 Hz, 1 H), 6.86−6.83 (m, 4H), 6.27 (d, J = 8.8 Hz, 4H), 2.68 (s, 12H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.0, 144.4, 142.6, 140.1, 138.7, 138.4, 135.4, 129.7, 129.6, 129.3, 127.9, 127.7, 122.0, 121.6, 119.5, 112.9, 111.8, 111.3, 40.3, 21.4; HRMS $[M + H]^+$ calculated for $C_{34}H_{32}N_4$ 497.2705, found 497.2707.

N,N,5′-Trimethyl-2′-(9H-pyrido[3,4-b]indol-1-yl)-[1,1′-biphenyl]-4-amine ***4bf***. White solid, Yield: 3.7 mg, 5%; R_f(PE/EA = 20/2) 0.45; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46 (d, J = 5.2 Hz, 1H), 7.96 (d, J = 7.7 Hz, 1H), 7.78 (d, J = 5.2 Hz, 1H), 7.57 (s, 1H), 7.51 (d, J = 7.8 Hz, 1H), 7.34−7.30 (m, 2H), 7.12−7.02 (m, 5H), 6.36−6.33 (m, 2H), 2.67 (s, 6H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, CDCl3) δ 148.6, 143.7, 139.3, 137.8, 132.7, 132.7, 130.5, 129.6, 128.2, 128.2, 127.7, 127.6, 127.5, 126.9, 126.7, 120.6, 120.5, 118.6, 112.3, 111.3, 110.1, 110.0, 39.2, 20.3; HRMS $[M + H]^+$ calculated for$C_{26}H_{23}N_3$ 378.1970, found 378.1972.

1-(4-Methyl-2,6-di(thiophen-2-yl)phenyl)-9H-pyrido[3,4-b]indole ***3bh***. Beige solid, Yield: 69.2 mg, 82%; R_f (PE/EA = 20/2) 0.45; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39 (d, J = 5.2 Hz, 1H), 8.00 (t, J = 7.4 Hz, 1H), 7.81 (d, J = 5.2 Hz, 1H), 7.71 (s, 1H), 7.40−7.36 (m, 1H) 7.26−7.22 (m, 2H), 7.15 (d, J = 7.1 Hz, 1H), 6.93 (dd, J = 5.08, 1.26 Hz, 2H), 6.61−6.53 (m, 5H), 2.45 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.9, 138.9, 135.4, 130.7, 128.2, 126.8, 126.8, 126.5, 125.7, 119.9, 114.3, 111.4, 21.3; HRMS $[M + H]^+$ calculated for $C_{26}H_{18}N_2S_2$ 423.0990, found 423.1021.

1-(4-Methyl-2-(thiophen-2-yl)phenyl)-9H-pyrido[3,4-b]indole ***4bh***. Beige solid, Yield: 8.1 mg, 12%; R_f (PE/EA = 20/2) 0.52; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.48 (d, J = 5.2 Hz, 1H), 8.02 (d, J = 7.7 Hz, 1H), 7.85 (d, J = 5.2 Hz, 1H), 7.70 (s, 1H), 7.49−7.42 (m, 2H), 7.39−7.35 (m, 1H), 7.25−7.23 (m, 1H), 7.18−7.14 (m, 2H), 6.94 (dd, J = 4.24 Hz, 2.04 Hz, 1H), 6.61−6.59 (m, 2H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.7, 142.1, 140.1, 139.4, 139.1, 134.3, 133.7, 133.0, 131.4, 130.8, 130.7, 129.0, 128.7, 128.2, 127.4, 126.8, 126.8, 126.5, 125.8, 125.7, 121.7, 121.6, 119.9, 113.9, 111.2, 21.3; HRMS $[M + H]^+$ calculated for $C_{22}H_{16}N_2S$ 341.1112, found 341.1114.

1-(5′-Methoxy-[1,1′:3′,1″-terphenyl]-2′-yl)-9H-pyrido[3,4-b]indole ***3ca***. White solid, Yield: 72.4 mg, 85%; R_f (PE/EA = 20/2) 0.7; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (d, J = 4 Hz, 1H), 7.91 (d, J = 8 Hz, 1H), 7.57 (m, 2H), 7.35 (t, J = 4 Hz, 1H), 7.21 (s, 1H), 7.13 (t, J = 8 Hz, 1H), 7.04−7.00 (m, 6H), 6.93 (m, 6H), 3.88 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.6, 144.2, 143.1, 140.9, 139.9, 138.7, 135.4, 129.1, 128.8, 128.0, 127.7, 127.6, 126.8, 121.7, 119.7, 115.2, 113.1, 111.2, 55.6; HRMS $[M + H]^+$ calculated for $C_{30}H_{22}N_2O$ 427.1810, found 427.1813.

1,1′-(5′-Methoxy-2′-(9H-pyrido[3,4-b]indol-1-yl)-[1,1′:3′,1″-terphenyl]-4,4″-diyl)diethanone ***3cd***. White solid, Yield: 82.6 mg, 81%; R_f (PE/EA = 20/2) 0.45; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (d, J = 4 Hz, 1H), 7.99 (d, J = 8 Hz, 2H), 7.69 (d, J = 4 Hz, 1H), 7.60−7.58 (d, J = 4 Hz, 4H), 7.45 (t, J = 6 Hz, 1H), 7.30−7.26 (m, 1H), 7.22−7.17 (m, 5H), 7.08−7.09 (d, J = 4 Hz, 2H), 3.92 (s, 3H), 2.41 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.7, 159.8, 145.5, 143.3, 140.1, 135.4, 135.4, 129.0, 128.5, 127.8, 121.9, 121.5, 120.2, 115.6, 113.8, 111.4, 55.7, 26.5; HRMS $[M + H]^+$ calculated for $C_{34}H_{26}N_2O_3$ 511.2022, found 511.2025.

1-(5′-Methoxy-2′-(9H-pyrido[3,4-b]indol-1-yl)-[1,1′-biphenyl]-4-yl)ethanone ***4cd***. White solid, Yield: 6.2 mg, 8%; R_f (PE/EA = 20/2) 0.5; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (d, J = 4 Hz, 1H), 8.00 (d, J = 8 Hz, 1H), 7.78 (m, 2H), 7.60−7.56 (m, 4H), 7.39 (t, J = 6 Hz, 1H), 7.22−7.19 (m, 2H), 7.03 (m, 3H), 3.85 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.6, 160.3, 145.5, 143.1, 141.1, 140.1, 139.1, 135.6, 134.0, 132.4, 129.4, 129.0, 128.9, 128.8, 128.4, 128.3, 128.2, 127.8, 121.8, 121.7, 121.6, 120.1, 115.9, 114.1, 113.9, 113.6, 111.2, 55.6, 26.5; HRMS $[M + H]^+$ calculated for $C_{26}H_{20}N_2O_2$ 393.1603, found 393.1605.

5′-Methoxy-N^4,N^4,$N^{4″}$,$N^{4″}$-tetramethyl-2′-(9H-pyrido[3,4-b]indol-1-yl)-[1,1′:3′,1″-terphenyl]-4,4″-diamine ***3cf***. White solid, Yield: 91.1 mg, 89%; R_f (PE/EA = 20/5) 0.47; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (d, J = 8 Hz, 1H), 8.04 (d, J = 8 Hz, 1H), 7.73 (s, 1H), 7.70 (d, J = 8 Hz, 1H), 7.47−7.43 (d, J = 8 Hz, 1H), 7.32 (d, J = 8 Hz, 1H), 7.23 (t, J = 6 Hz, 1H), 7.03 (s, 2H), 6.98 (d, J = 8 Hz, 4H), 6.39 (d, J = 8 Hz, 4H), 3.95 (s, 3H), 2.79 (s, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.5, 149.1, 144.3, 144.2, 140.1, 138.8, 135.6, 129.6, 129.2, 127.8, 127.7, 127.2, 122.0, 121.6, 119.5, 114.3, 114.2, 113.8, 112.9, 111.8, 111.7, 111.3, 55.4, 40.3; HRMS $[M + H]^+$ calculated for $C_{34}H_{32}N_4O$ 513.2654, found 513.2679.

2′-(9H-Pyrido[3,4-b]indol-1-yl)-[1,1′:3′,1″-terphenyl]-5′-carbonitrile ***3da***. White solid, Yield: 77.4 mg, 92%; R_f (PE/EA = 20/2) 0.4; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, J = 5.2 Hz, 1H), 7.93 (d, J = 7.8 Hz, 1H), 7.76 (s, 2H), 7.63 (d, J = 5.2 Hz, 1H), 7.41−7.37 (m, 1H), 7.24 (d, J = 8.2 Hz, 1H), 7.16−7.13 (m, 2H), 6.97 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.2, 140.1, 138.8, 138.7, 134.7, 132.8, 128.6, 128.4, 128.0, 127.6, 121.7, 121.4, 120.1, 114.0, 111.3; HRMS $[M + H]^+$ calculated for $C_{30}H_{19}N_3$ 422.1657, found 422.1648.

4,4″-Diacetyl-2′-(9H-pyrido[3,4-b]indol-1-yl)-[1,1′:3′,1″-terphenyl]-5′-carbonitrile ***3dd***. White solid, Yield: 92.9 mg, 92%; R_f (PE/EA = 20/2) 0.40; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, J = 5.3 Hz, 1H), 7.92 (d, J = 7.8 Hz, 1H), 7.62 (d, J = 4.9 Hz, 2H), 7.53, (d, J = 8.4 Hz, 4H), 7.39−7.35 (m, 1H), 7.3 (s, 2H), 7.21 (d, J = 8.2 Hz, 1H), 7.16−7.14 (m, 1H), 7.10 (d, J = 8.4 Hz, 4H), 2.35 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.4, 140.8, 139.9, 139.6, 138.0, 137.8, 136.7, 135.9, 132.9, 129.9, 129.5, 128.9, 128.6, 128.3, 127.9, 121.6, 121.2, 120.2, 114.5, 111.2, 26.5; HRMS $[M + H]^+$ calculated for $C_{34}H_{23}N_3O_2$ 506.1869, found 506.1870.

4,4″-Dimethoxy-2′-(9H-pyrido[3,4-b]indol-1-yl)-[1,1′:3′,1″-terphenyl]-5′-carbonitrile ***3de***. White solid, Yield: 85.6 mg, 89%; R_f (PE/EA = 20/2) 0.45; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (d, J = 4 Hz, 1H), 7.95 (d, J = 8 Hz, 1H), 7.69−7.65 (m, 4H), 7.42−7.38 (t, J = 8 Hz, 1H), 7.25−7.14 (m, 2H), 6.90−6.88 (dd, J = 8 Hz, 4H), 6.49−6.47 (dd, J = 8 Hz, 4H), 3.55 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.9, 143.8, 141.5, 140.1, 139.3, 138.9, 134.6, 132.4, 131.1, 129.9, 128.7, 128.4, 121.8, 121.5, 120.1, 110.6, 113.5, 112.9, 111.4, 55.0; HRMS $[M + H]^+$ calculated for $C_{32}H_{23}N_3O_2$ 482.1869, found 482.1870.

4,4″-Bis(dimethylamino)-2′-(9H-pyrido[3,4-b]indol-1-yl)-[1,1′:3′,1″-terphenyl]-5′-carbonitrile ***3df***. White solid, Yield: 90.2 mg, 89%; R_f (PE/EA = 20/5) 0.51; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (d, J = 4 Hz, 1H), 8.03 (d, J = 8 Hz, 1H), 8.017 (m, 1H), 7.75 (d, J = 4 Hz, 2H), 7.48−7.44 (t, J = 8 Hz, 2H), 7.34 (d, J = 12 Hz, 1H), 7.24−7.22 (m, 2H), 6.90 (d, J = 8 Hz, 3H), 6.35 (d, J = 8 Hz, 3H), 2.77 (s, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.5, 144.3, 134.8, 131.9, 129.5, 129.2, 126.5, 121.7, 121.6, 120.0, 113.8, 112.3, 111.8, 111.6, 40.1; HRMS $[M + H]^+$ calculated for $C_{34}H_{29}N_5$ 508.2501, found 508.2504.

DOI: 10.1021/acs.joc.5b00411
J. Org. Chem. 2015, 80, 5532−5545

4-(9H-Pyrido[3,4-b]indol-1-yl)-3,5-di(thiophen-2-yl)benzonitrile ***3dh***. Beige solid, Yield: 70.1 mg, 81%; R_f (PE/EA = 20/2) 0.54; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (d, J = 8 Hz, 1H), 8.02 (d, J = 8 Hz, 1H), 7.88 (m, 3H), 7.73 (s, 1H), 7.44 (t, J = 8 Hz, 1H), 7.34 (d, J = 8 Hz, 1H), 7.21 (m, 1H), 6.99 (dd, J = 8 Hz, 2H), 6.65 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.3, 139.2, 137.3, 132.5, 128.6, 128.0, 127.4, 127.1, 121.8, 120.3, 115.2, 111.5; HRMS [M + H]$^+$ calculated for $C_{26}H_{15}N_3S_2$ 434.0786, found 434.0779.

1-(5′-Fluoro-[1,1′:3′,1″-terphenyl]-2′-yl)-9H-pyrido[3,4-b]indole ***3ea***. White solid, Yield: 74.5 mg, 90%; R_f (PE/EA = 20/1) 0.50; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, J = 4 Hz, 1H), 7.92 (d, J = 8 Hz, 1H), 7.6 (d, J = 8 Hz, 1H), 7.57 (s, 1H), 7.38 (m, 1H), 7.22−7.18 (m, 3H), 7.14 (t, J = 8 Hz, 1H), 7.00 (m, 4H), 6.94 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.8 (d, J_{C-F} = 247 Hz), 145.1, 145.0, 142.2, 140.0, 139.9, 139.8, 138.8, 135.2, 128.7, 127.8, 127.2, 121.7, 121.4, 119.9, 116.5 (d, J_{C-F} = 21 Hz), 113.5, 111.2; HRMS [M + H]$^+$ calculated for $C_{29}H_{19}FN_2$ 415.1611, found 415.1613.

1,1′-(5′-Fluoro-2′-(9H-pyrido[3,4-b]indol-1-yl)-[1,1′:3′,1″-terphenyl]-4,4″-diyl)diethanone ***3ed***. White solid, Yield: 88.6 mg, 89%; R_f (PE/EA = 20/5) 0.52; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.48 (d, J = 5.2 Hz, 1H), 7.93 (d, J = 7.8 Hz, 1H), 7.72 (s, 1H), 7.63 (d, J = 5.2 Hz, 1H), 7.55−7.53 (m, 4H), 7.41−7.36 (m, 2H), 7.23 (t, J = 7.0 Hz, 3H), 7.10−7.08 (m, 4H), 2.36 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.6, 163.8 (d, J_{C-F} = 249.0 Hz), 144.1 (3C), 140.0, 138.9, 135.7, 135.1, 132.0 (2C), 132.0, 128.9, 128.5, 127.9, 121.8, 121.5, 120.3, 117.0 (d, J_{C-F} = 22 Hz), 114.1, 111.4, 26.5; HRMS [M + H]$^+$ calculated for $C_{33}H_{23}FN_2O_2$ 499.1822, found 499.1820.

1-(5′-Fluoro-4,4″-dimethoxy-[1,1′:3′,1″-terphenyl]-2′-yl)-9H-pyrido[3,4-b]indole ***3ee***. White solid, Yield: 85.3 mg, 90%; R_f (PE/EA = 20/2) 0.56; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, J = 5.2 Hz, 1H), 7.95 (d, J = 7.8 Hz, 1H), 7.63 (d, J = 5.2 Hz, 1H), 7.59 (s, 1H), 7.40−7.36 (m, 1H), 7.25−7.22 (m, 2H), 7.14−7.12 (m, 3H), 6.92−6.88 (m, 4H), 6.48−6.44 (m, 3H), 3.54 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.6, 144.6, 144.6, 140.0, 138.8, 135.2, 132.3, 130.6, 129.9, 128.3, 121.7, 119.9, 116.0, 115.8, 115.5, 113.4, 113.3, 55.0; HRMS [M + H]$^+$ calculated for $C_{31}H_{23}FN_2O_2$ 475.1822, found 475.1820.

5′-Fluoro-N^4,N^4,N$^{4″}$,N$^{4″}$-tetramethyl-2′-(9H-pyrido[3,4-b]indol-1-yl)-[1,1′:3′,1″-terphenyl]-4,4″-diamine ***3ef***. White solid, Yield: 90.0 mg, 90%; R_f (PE/EA = 20/2) 0.40; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (d, J = 4 Hz, 1H), 8.02 (d, J = 8 Hz, 1H), 7.74 (s, 1H), 7.71 (d, J = 8 Hz, 1H), 7.45−7.41(t, J = 8 Hz, 1H), 7.31 (d, J = 8 Hz, 1H), 7.22−7.14 (m, 3H), 6.91 (d, J = 8 Hz, 4H), 6.34 (d, J = 8 Hz, 4H), 2.76 (s, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.9 (d, J_{C-F} = 246 Hz), 149.3, 145.1, 145.0, 140.3, 135.4, 129.5, 127.9, 121.7, 119.7, 115.4, 115.2, 113.3, 111.7, 111.5, 40.2; HRMS [M + H]$^+$ calculated for $C_{33}H_{29}FN_4$ 501.2455, found 501.2453.

1-(4-Fluoro-2,6-di(thiophen-2-yl)phenyl)-9H-pyrido[3,4-b]indole ***3eh***. White solid, Yield: 74.9 mg, 88%; R_f (PE/EA = 20/1) 0.52; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.26 (s, 1H), 8.44 (d, J = 5.1 Hz, 2H), 8.29 (s, 2H), 8.25 (d, J = 7.8 Hz, 1H), 8.18 (d, J = 5.0 Hz, 1H), 7.71 (s, 1H), 7.51 (t, J = 7.3 Hz, 1H), 7.45 (d, J = 8.1 Hz, 1H), 7.31 (dd, J = 5.06 Hz, 1.06 Hz, 2H), 7.26 (t, J = 7.3 Hz, 1H), 6.93 (dd, J = 3.6 Hz, 1.0 Hz, 2H), 6.84 (dd, J = 5.0 Hz, 3.7 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 166.9, 141.1, 140.6, 135.6, 135.2, 134.7, 128.0, 127.1, 126.6, 121.7, 120.5, 119.2, 111.9; HRMS [M + H]$^+$ calculated for $C_{25}H_{15}FN_2S_2$ 427.0739, found 427.0740.

1-(5′-Nitro-2′-(9H-pyrido[3,4-b] indol-1-yl)-[1,1′-biphenyl]-4-yl)-ethanone ***4fd***. Yellow solid, Yield: 26.0 mg, 32%; R_f (PE/EA = 20/2) 0.51; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (d, J = 4 Hz, 1H), 8.40 (d, J = 2.4 Hz, 1H), 8.35−8.32 (dd, J = 8 Hz, 1H), 8.02 (d, J = 8 Hz, 1H), 7.89 (m, 2H), 7.69 (s, 1H), 7.66 (d, J = 8 Hz, 2H), 7.43−7.39 (t, J = 8 Hz, 1H), 7.26−7.20 (m, 4H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.3, 148.3, 143.2, 143.1, 141.3, 140.8, 140.1, 139.7, 136.3, 133.5, 132.6, 129.7, 129.0, 128.8, 128.5, 125.4, 123.2, 121.9, 121.3, 120.6, 114.8, 111.3, 26.5; HRMS [M + H]$^+$ calculated for $C_{25}H_{17}N_3O_3$ 408.1348, found 408.1350.

1-(4,4″-Dimethoxy-5′-nitro-[1,1′:3′,1″-terphenyl]-2′-yl)-9H-pyrido[3,4-b]indole ***3fe***. Pale yellow solid, Yield: 43.0 mg, 43%; R_f (PE/EA = 20/2) 0.55; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (m, 2H), 7.96 (d, J = 8 Hz, 1H), 7.88 (m, 1H), 7.68 (d, J = 4 Hz, 1H), 7.42 (m, 1H), 7.25 (m, 1H), 7.14 (m, 2H), 6.95 (m, 4H), 6.51 (m, 4H), 3.56 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.0, 144.3, 140.1, 139.0, 134.6, 131.2, 129.9, 129.7, 128.8, 123.7, 121.8, 121.5, 120.2, 114.0, 113.6, 111.4, 55.1; HRMS [M + H]$^+$ calculated for $C_{31}H_{23}N_3O_4$ 502.1767, found 502.1769.

1-(4′-Methoxy-5-nitro-[1,1′-biphenyl]-2-yl)-9H-pyrido[3,4-b]-indole ***4fe***. Yellow solid, Yield: 33.2 mg, 42%; R_f (PE/EA = 20/1) 0.52; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51 (d, J = 8 Hz, 1H), 8.38 (d, J = 4 Hz, 1H), 8.27 (dd, J = 8 Hz, 1H), 8.01 (d, J = 8 Hz, 1H), 7.88 (d, J = 4 Hz, 1H), 7.85 (d, J = 8 Hz, 1H), 7.48 (s, 1H), 7.41−7.37 (t, J = 8 Hz, 1H), 7.19−7.12 (m, 4H), 6.61−6.58 (m, 2H), 3.56 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.6, 148.3, 142.9, 141.6, 141.5, 140.2, 139.7, 133.3, 133.0, 130.8, 129.7, 129.6, 128.7, 125.1, 122.0, 121.7, 121.3, 120.3, 114.6, 114.3, 111.2, 55.2; HRMS [M + H]$^+$ calculated for $C_{24}H_{17}N_3O_3$ 396.1348, found 396.1350.

N^4,N^4,N$^{4″}$,N$^{4″}$-Tetramethyl-5′-nitro-2′-(9H-pyrido[3,4-b]indol-1-yl)-[1,1′:3′,1″-terphenyl]-4,4″-diamine ***3ff***. Yellow solid, Yield: 42.1 mg, 40%; R_f (PE/EA = 20/5) 0.49; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (d, J = 8 Hz, 1H), 8.21 (s, 2H), 7.97 (d, J = 8 Hz, 1H), 7.68 (d, J = 8 Hz, 1H), 7.64 (s, 1H), 7.38 (t, J = 4 Hz, 1H), 7.25 (d, J = 8 Hz, 1H), 7.17 (t, J = 6 Hz, 1H), 6.87 (d, J = 8 Hz, 4H), 6.30 (d, J = 8 Hz, 4H), 2.71 (s, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.6, 148.0, 144.7, 142.2, 140.3, 140.1, 139.0, 134.8, 129.6, 128.6, 128.2, 126.7, 123.0, 121.7, 121.7, 119.9, 113.8, 111.8, 111.5, 40.1; HRMS [M + H]$^+$ calculated for $C_{33}H_{29}N_5O_2$ 528.2400, found 528.2402.

N,N-Dimethyl-5′-nitro-2′-(9H-pyrido[3,4-b]indol-1-yl)-[1,1′-biphenyl]-4-amine ***4ff***. Yellow solid, Yield: 39.1 mg, 48%; R_f (PE/EA = 20/2) 0.35; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (d, J = 8 Hz, 1H), 8.37 (d, J = 4 Hz, 1H), 8.19 (dd, J = 8 Hz, 1H), 8.00 (d, J = 8 Hz, 1H), 7.88 (d, J = 4 Hz, 1H), 7.82 (d, J = 8 Hz, 1H), 7.48 (s, 1H), 7.39−7.35 (t, J = 8 Hz, 1H), 7.17 (m, 2H), 7.09−7.06 (dd, J = 6 Hz, 2H), 6.38−6.36 (d, J = 8 Hz, 2H), 2.72 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.3, 148.3, 142.7, 142.2, 141.9, 140.4, 139.7, 133.3, 133.2, 129.5, 129.2, 128.5, 125.6, 124.8, 121.6, 121.3, 121.2, 120.1, 114.5, 112.3, 111.3, 40.1; HRMS [M + H]$^+$ calculated for $C_{25}H_{20}N_4O_2$ 409.1665, found 409.1667.

5′-Nitro-2′-(9H-pyrido[3,4-b]indol-1-yl)-[1,1′-biphenyl]-4-carbonitrile ***4fg***. Pale yellow solid, Yield: 31.9 mg, 41%; R_f (PE/EA = 20/2) 0.45; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37−8.30 (m, 3H), 8.06 (d, J = 8 Hz, 1H), 7.91−7.87 (m, 2H), 7.49 (t, J = 8 Hz, 1H), 7.36−7.34 (d, J = 8 Hz, 2H), 7.32−7.23 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.2, 142.0, 140.0, 132.6, 131.3, 131.2, 128.4, 124.4, 122.5, 121.0, 120.1, 120.0, 117.1, 114.1, 110.9, 110.5; HRMS [M + H]$^+$ calculated for $C_{24}H_{14}N_4O_2$ 391.1195, found 391.1197.

1-(3-Phenylthiophen-2-yl)-9H-pyrido[3,4-b]indole ***6a***. Beige solid, Yield: 61.9 mg, 95%; R_f (PE/EA = 20/1) 0.53; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.48 (s, 1H), 7.96 (br, 1H), 7.83 (br, 1H), 7.51−6.93 (m, 11H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.0, 139.5, 138.9, 136.5, 131.5, 130.1, 130.0, 129.9, 129.1, 128.4, 128.3, 127.9, 121.5, 121.1, 120.0, 114.2, 111.1; HRMS [M + H]$^+$ calculated for $C_{21}H_{14}N_2S$ 327.0956, found 327.0958.

1-(3-(4-(tert-Butyl)phenyl)thiophen-2-yl)-9H-pyrido[3,4-b]indole ***6b***. Beige solid, Yield: 68.7 mg, 90%; R_f (PE/EA = 20/1) 0.54; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.48 (d, J = 8 Hz, 1H), 7.97 (d, J = 7.8 Hz, 1H), 7.83 (d, J = 4 Hz, 1H), 7.50−7.48 (d, J = 8 Hz, 1H), 7.31−7.18 (m, 5H), 7.12−7.07 (m, 2H), 6.85 (d, J = 8 Hz, 1H), 1.15 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.3, 138.9, 138.3, 137.6, 137.0, 136.3, 132.6, 131.1, 129.0, 128.9, 127.1, 126.9, 125.0, 120.4, 120.0, 118.9, 113.0, 109.9, 30.2, 28.7; HRMS [M + H] $^+$ calculated for $C_{25}H_{22}N_2S$ 383.1582, found 383.1580.

1-(3-(Naphthalen-2-yl)thiophen-2-yl)-9H-pyrido[3,4-b]indole ***6c***. White solid, Yield: 66.9 mg, 89%; R_f (PE/EA = 20/1) 0.52; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50 (d, J = 5.2 Hz, 1H), 7.93 (d, J = 8 Hz, 2H), 7.87−7.83 (m, 1H), 7.68 (dd, J = 3.6, 1.3 Hz, 1H), 7.65−7.62 (m, 1H), 7.56−7.54 (d, J = 5.2 Hz, 1H), 7.51−7.48 (m, 1H), 7.37−7.35 (m, 2H), 7.31 (d, J = 1.6 Hz, 1H), 7.21−7.16 (m, 2H), 7.10−7.04 (m, 1H), 6.67 (d, J = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.8, 139.5, 139.0, 132.9, 133.4, 132.7, 132.5, 130.2, 128.7, 128.3, 127.9, 127.7, 126.9, 126.6, 126.3, 125.0, 121.5, 121.1, 120.6, 120.0, 114.2, 111.7, 110.0; HRMS [M + H]$^+$ calculated for $C_{25}H_{16}N_2S$ 377.1112, found 377.1110.

1-(4-(2-(9H-Pyrido[3,4-b]indol-1-yl)thiophen-3-yl)phenyl)-ethanone ***6d***. Beige solid, Yield: 61.1 mg, 83%; R_f (PE/EA = 20/5)

DOI: 10.1021/acs.joc.5b00411
J. Org. Chem. 2015, 80, 5532−5545

0.55; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.48 (d, J = 4 Hz, 1H), 8.00 (d, J = 8 Hz, 1H), 7.87 (d, J = 4 Hz, 1H), 7.73 (d, J = 8 Hz, 2H), 7.53 (d, J = 4 Hz, 1H), 7.44 (s, 1H), 7.38−7.13 (m, 5H), 7.02 (d, J = 8 Hz, 1H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.4, 140.8, 139.9, 139.6, 138.0, 137.8, 136.7, 135.9, 132.9, 129.9, 129.6, 128.9, 128.7, 128.3, 128.0, 121.7, 121.3, 120.3, 114.5, 111.2, 26.6; HRMS [M + H]$^+$ calculated for $C_{23}H_{16}N_2OS$ 369.1062, found 369.1060.

1-(3-(4-Methoxyphenyl)thiophen-2-yl)-9H-pyrido[3,4-b]indole **6e**. White solid, Yield: 62.6 mg, 88%; R_f (PE/EA = 20/2) 0.60; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (br, 1H), 7.98 (d, J = 4 Hz, 1H), 7.83 (br, 1H), 7.47−6.96 (m, 8H), 6.71 (d, J = 4 Hz, 2H), 3.63 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.3, 140.0, 139.4, 138.5, 137.5, 136.8, 132.2, 130.0, 129.8, 129.5, 128.7, 128.4, 127.8, 121.5, 121.2, 120.0, 115.7, 114.5, 114.1, 111.2, 55.3; HRMS [M + H]$^+$ calculated for $C_{22}H_{16}N_2OS$ 357.1062, found 357.1060.

4-(2-(9H-Pyrido[3,4-b]indol-1-yl)thiophen-3-yl)-N,N-dimethylaniline **6f**. Beige solid, Yield: 61.2 mg, 83%; R_f (PE/EA = 20/5) 0.45; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (d, J = 4 Hz, 1H), 7.98 (d, J = 8 Hz, 1H), 7.83 (d, J = 8 Hz, 1H), 7.47 (d, J = 8 Hz, 1H), 7.34−7.31 (m, 2H), 7.22−7.19 (m, 2H), 7.14−7.10 (t, J = 8 Hz, 1H), 6.95 (d, J = 8 Hz, 1H), 6.53 (d, J = 8 Hz, 2H), 2.80 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.2, 140.2, 139.3, 130.1, 129.2, 128.2, 127.7, 121.4, 119.8, 113.8, 112.7, 111.2, 40.4; HRMS [M + H]$^+$ calculated for $C_{23}H_{19}N_3S$ 370.1378, found 370.1376.

4-(2-(9H-Pyrido[3,4-b]indol-1-yl)thiophen-3-yl)benzonitrile **6g**. Beige solid, Yield: 54.0 mg, 77%; R_f (PE/EA = 20/2) 0.55; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (d, J = 4 Hz, 1H), 8.13 (d, J = 8 Hz, 1H), 7.99 (d, J = 4 Hz, 1H), 7.65 (d, J = 4 Hz, 1H), 7.61 (s, 1H), 7.52−7.44 (m, 5H), 7.38 (d, J = 8 Hz, 1H), 7.31 (d, J = 8 Hz, 1H), 7.22 (d, J = 8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.6, 139.9, 139.8, 137.8, 137.5, 136.2, 133.1, 132.5, 130.0, 129.3, 128.9, 128.7, 128.0, 121.8, 121.3, 120.6, 118.5, 114.7, 111.2, 111.1; HRMS [M + H]$^+$ calculated for $C_{22}H_{13}N_3S$ 352.0908, found 352.0906.

1-([2,3′-Bithiophen]-2′-yl)-9H-pyrido[3,4-b]indole **6h**. Beige solid, Yield: 53.7 mg, 81%; R_f (PE/EA = 20/2) 0.52; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51 (d, J = 5.2 Hz, 1H), 8.03 (d, J = 7.6 Hz, 1H), 7.89 (d, J = 5.2 Hz, 1H), 7.62 (s, 1H), 7.48 (d, J = 5.2 Hz, 1H), 7.39 (t, J = 7.6 Hz, 1H), 7.27 (d, J = 5.2 Hz, 1H), 7.20−7.08 (m, 3H), 6.86 (d, J = 3.5 Hz, 1H), 6.80 (t, J = 4.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.1, 139.6, 137.4, 136.9, 136.7, 133.3, 131.7, 129.8, 129.7, 128.6, 127.8, 126.5, 126.0, 121.7, 121.3, 120.2, 114.5, 111.3; HRMS [M + H]$^+$ calculated for $C_{19}H_{12}N_2S_2$ 333.0520, found 333.0522.

1-(3-(Pyridin-3-yl)thiophen-2-yl)-9H-pyrido[3,4-b]indole **6i**. Beige solid, Yield: 51.0 mg, 78%; R_f (PE/EA = 20/10) 0.49 ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (br, 1H), 8.47 (d, J = 4 Hz, 1H), 8.32 (br, 1H), 8.01 (d, J = 4 Hz, 1H), 7.70 (br, 1H), 7.55 (d, J = 4 Hz, 1H), 7.47 (d, J = 8 Hz, 1H), 7.39−7.35 (t, J = 8 Hz, 1H), 7.28 (d, J = 4 Hz, 2H), 7.17−6.98 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.9, 148.6, 140.0, 139.7, 137.4, 136.4, 135.8, 135.3, 133.0, 130.0, 129.3, 128.7, 128.0, 121.7, 121.4, 120.4, 114.6, 111.3; HRMS [M + H]$^+$ calculated for $C_{20}H_{13}N_3S$ 328.0908, found 328.0910.

1-(3-Phenylnaphthalen-2-yl)-9H-pyrido[3,4-b]indole **8a**. Beige solid, Yield: 38.4 mg, 52%; R_f (PE/EA = 20/1) 0.68; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53−8.51 (d, J = 8 Hz, 1H), 8.23 (s, 1H), 8.07 (d, J = 4 Hz, 2H), 7.98−7.94 (t, J = 8 Hz, 2H), 7.89 (d, J = 4 Hz, 1H), 7.73 (s, 1H), 7.59−7.55 (m, 2H), 7.46−7.42 (t, J = 8 Hz, 1H), 7.31−7.22 (m, 4H), 7.13- 7.06 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.7, 139.3, 138.5, 133.6, 132.7, 130.8, 129.6, 128.8, 128.2, 128.1, 127.9, 127.1, 127.0, 126.6, 121.7, 121.5, 120.0, 113.7, 111.1; HRMS [M + H]$^+$ calculated for $C_{27}H_{18}N_2$ 371.1548, found 371.1548.

1-(4-(3-(9H-Pyrido[3,4-b]indol-1-yl)naphthalen-2-yl)phenyl)-ethanone **8d**. Beige solid, Yield: 53.7 mg, 65%; R_f (PE/EA = 20/5) 0.53; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46 (d, J = 8 Hz, 1H), 8.21 (s, 1H), 8.11 (d, J = 8 Hz, 1H), 8.05 (s, 1H), 7.97−7.91 (m, 3H), 7.71 (d, J = 8 Hz, 2H), 7.62−7.47 (m, 5H), 7.34−7.27 (m, 3H), 2.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.7, 137.6, 135.4, 134.2, 133.5, 132.8, 130.7, 130.1, 129.1, 128.9, 128.2, 128.1, 128.0, 127.4, 127.2, 122.0, 121.5, 120.4, 114.0, 111.4, 26.5; HRMS [M + H]$^+$ calculated for $C_{29}H_{20}N_2O$ 413.1654, found 413.1652.

1,1′-((2-(9H-Pyrido[3,4-b]indol-1-yl)naphthalene-1,3-diyl)bis(4,1-phenylene))diethanone **9d**. Beige solid, Yield: 2.1 mg, 2%; R_f (PE/EA = 20/5) 0.42; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (d, J = 8 Hz, 1H), 7.97 (s, 1H), 7.94 (dd, J = 12 Hz, 2H), 7.70−7.68 (dd, J = 8 Hz, 1H), 7.57−7.47 (m, 7H), 7.41 (d, J = 8 Hz, 2H), 7.39−7.35 (t, J = 8 Hz, 2H), 7.24 (d, J = 8 Hz, 2H), 7.15−7.11(t, J = 8 Hz, 1H), 7.04 (d, J = 8 Hz, 1H), 2.37 (s, 3H), 2.33 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.8, 145.4, 143.1, 140.0, 138.4, 135.6, 135.3, 135.0, 133.5, 131.8, 129.7, 129.3, 128.4, 127.8, 127.7, 127.4, 127.2, 126.5, 121.9, 121.5, 120.2, 113.7, 111.3, 26.5, 26.4; HRMS [M + H]$^+$ calculated for $C_{37}H_{26}N_2O_2$ 531.2073, found 531.2073.

1-(Pyren-1-yl)-9H-pyrido[3,4-b]indole **10**. Yellow solid, Yield: 47.8 mg, 65%; R_f (PE/EA = 20/1) 0.45; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.73 (d, J = 8 Hz, 1H), 8.37 (d, J = 8 Hz, 1H), 8.32 (d, J = 8 Hz, 1H), 8.27−8.17 (m, 5H), 8.10 (d, J = 8 Hz, 1H), 8.07−7.98 (m, 3H), 7.53 (t, J = 8 Hz, 1H), 7.34 (d, J = 8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.2, 139.8, 132.5, 131.8, 131.4, 130.9, 128.7, 128.6, 128.4, 128.1, 127.6, 127.5, 126.2, 125.6, 125.4, 125.2, 124.7, 121.9, 120.3, 114.0, 111.5; HRMS [M + H]$^+$ calculated for $C_{27}H_{16}N_2$ 369.1392, found 369.1376.

1-(4-(1-(9H-Pyrido[3,4-b]indol-1-yl)pyren-2-yl)phenyl)ethanone **11d**. Yellow white solid, Yield: 68.0 mg, 70%; R_f (PE/EA = 20/5) 0.57; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50 (d, J = 4 Hz, 1H), 8.27 (s, 1H), 8.21 (d, J = 8 Hz, 1H), 8.15−8.06 (m, 4H), 8.01 (t, J = 8 Hz, 1H), 7.91−7.88 (m, 2H), 7.61−7.55 (m, 3H), 7.40−7.32 (m, 3H), 7.22 (d, J = 8 Hz, 2H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.8, 146.3, 138.7, 135.8, 135.2, 131.9, 131.3, 130.8, 130.3, 129.9, 128.9, 128.8, 128.6, 127.9, 127.3, 126.6, 126.5, 125.9, 125.7, 124.9, 124.4, 122.0, 121.7, 120.3, 114.2, 111.5, 26.5; HRMS [M + H]$^+$ calculated for $C_{35}H_{22}N_2O$ 487.1810, found 487.1808.

1-Phenyl-9H-carbazole **13**. White solid, Yield: 18.2 mg, 38%; R_f (PE/EA = 20/1) 0.65; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (br s, 1H), 8.04 (m, 2H), 7.63 (m, 2H), 7.50 (m, 2H), 7.38 (m, 4H), 7.27 (t, J = 8 Hz, 1H), 7.18 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.5, 139.1, 137.3, 129.2, 128.4, 127.6, 126.0, 125.7, 125.1, 123.7, 123.6, 120.5, 119.9, 119.6, 119.5, 110.7; HRMS [M + H]$^+$ calculated for $C_{18}H_{14}N$ 244.1126, found 244.1122.

■ ASSOCIATED CONTENT

Supporting Information

Details for experiment conditions, copies of ^{1}H and ^{13}C NMR spectra for all isolated compounds, and single crystal data of **2cr**. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: velan.g@vit.ac.in.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This activity is supported by DST (SR/FT/CS-135/2011) and VIT University, Vellore. Instrumental facility provided by VIT-SIF and XRD Lab, SAIF-IITM, Chennai is gratefully acknowledged. T.G. sincerely thanks Johnson Matthey Chemicals India Private Ltd. for gifting Pd/C.

■ REFERENCES

(1) (a) *Modern Arylation Methods*, 1st ed.; Ackermann, L., Ed.; Wiley-VCH: Weinheim, 2009. (b) *Handbook of C-H Transformations*; Dyker, G., Ed.; Wiley-VCH: Weinheim, 2005. (c) Dixneuf, P. H.; Cadierno, V. *Metal-Catalyzed Reactions in Water*; Wiley-VCH: Weinheim, 2013. (d) Ackermann, L.; Vicente, R.; Kapdi, A. R. *Angew. Chem., Int. Ed.* **2009**, *48*, 9792. (e) Wencel-Delord, J.; Glorius, F. *Nat. Chem.* **2013**, *5*, 369. (f) Oi, S.; Fukita, S.; Hirata, N.; Watanuki, N.; Miyano, S.; Inoue, Y. *Org. Lett.* **2001**, *3*, 2579. (g) Ackermann, L. *Chem. Rev.* **2011**, *111*, 1315. (h) Rossi, R.; Bellina, F.; Lessi, M.; Manzini, C. *Adv. Synth. Catal.* **2014**,

DOI: 10.1021/acs.joc.5b00411
J. Org. Chem. 2015, 80, 5532−5545

356, 17. (i) Arockiam, P. B.; Bruneau, C.; Dixneuf, P. H. *Chem. Rev.* **2012**, *112*, 5879.
(2) (a) Yamaguchi, J.; Yamaguchi, A. D.; Itami, K. *Angew. Chem., Int. Ed.* **2012**, *51*, 8960. (b) McMurray, L.; O'Hara, F.; Gaunt, M. J. *Chem. Soc. Rev.* **2011**, *40*, 1885. (c) Chen, D. Y. K.; Youn, S. W. *Chem.—Eur. J.* **2012**, *18*, 9452. (d) Yaşar, S.; Doğan, Ö.; Özdemir, I.; Çetinkaya, B. *Appl. Organomet. Chem.* **2008**, *22*, 314.
(3) (a) Lakshman, M. K.; Deb, A. C.; Chamala, R. R.; Pradhan, P.; Pratap, R. *Angew. Chem., Int. Ed.* **2011**, *50*, 11400. (b) Guo, H.-M.; Jiang, L.-L.; Niu, H.-Y.; Rao, W.-H.; Liang, L.; Mao, R.-Z.; Li, D.-Y.; Qu, G.-R. *Org. Lett.* **2011**, *13*, 2008.
(4) (a) Ishida, J.; Wang, H.-K.; Bastow, K. F.; Hu, C.-Q.; Lee, K.-H. *Bioorg. Med. Chem. Lett.* **1999**, *9*, 3319. (b) Yu, X.; Lin, W.; Li, J.; Yang, M. *Bioorg. Med. Chem. Lett.* **2004**, *14*, 3127. (c) Chen, Y.-F.; Kuo, P.-C.; Chan, H.-H.; Kuo, I. J.; Lin, F.-W.; Su, C.-R.; Yang, M.-L.; Li, D.-T.; Wu, T.-S. *J. Nat. Prod.* **2010**, *73*, 1993. (d) Ishida, J.; Wang, H.-K.; Oyama, M.; Cosentino, M. L.; Hu, C.-Q.; Lee, K.-H. *J. Nat. Prod.* **2001**, *64*, 958. (e) Winkler, J. D.; Londregan, A. T.; Hamann, M. T. *Org. Lett.* **2006**, *8*, 2594. (f) Tsuda, M.; Watanabe, D.; Kobayashi, J. i. *Tetrahedron Lett.* **1998**, *39*, 1207.
(5) (a) Tu, L. C.; Chen, C.-S.; Hsiao, I. C.; Chern, J.-W.; Lin, C.-H.; Shen, Y.-C.; Yeh, S. F. *Chem. Biol.* **2005**, *12*, 1317. (b) Li, Y.; Zhao, M.; Parkin, K. L. *J. Agric. Food Chem.* **2011**, *59*, 2332. (c) Liew, L. P. P.; Fleming, J. M.; Longeon, A.; Mouray, E.; Florent, I.; Bourguet-Kondracki, M.-L.; Copp, B. R. *Tetrahedron* **2014**, *70*, 4910.
(6) Wu, N.; Song, F.; Yan, L.; Li, J.; You, J. *Chem.—Eur. J.* **2014**, *20*, 3408.
(7) (a) Ackermann, L.; Diers, E.; Manvar, A. *Org. Lett.* **2012**, *14*, 1154. (b) Ma, W.; Ackermann, L. *Chem.—Eur. J.* **2013**, *19*, 13925. (c) Li, B.; Darcel, C.; Dixneuf, P. H. *ChemCatChem* **2014**, *6*, 127. (d) Raghuvanshi, K.; Rauch, K.; Ackermann, L. *Chem.—Eur. J.* **2015**, *21*, 1790.
(8) (a) Demir, S.; Özdemir, I.; Çetinkaya, B. *J. Organomet. Chem.* **2009**, *694*, 4025. (b) Luo, N.; Yu, Z. *Chem.—Eur. J.* **2010**, *16*, 787. (c) Yu, B.; Yan, X.; Wang, S.; Tang, N.; Xi, C. *Organometallics* **2010**, *29*, 3222. (d) Doherty, S.; Knight, J. G.; Addyman, C. R.; Smyth, C.; Ward, N. A. B.; Harrington, R. W. *Organometallics* **2011**, *30*, 6010. (e) Li, W.; Yin, Z.; Jiang, X.; Sun, P. *J. Org. Chem.* **2011**, *76*, 8543. (f) Kim, H. J.; Ajitha, M. J.; Lee, Y.; Ryu, J.; Kim, J.; Lee, Y.; Jung, Y.; Chang, S. *J. Am. Chem. Soc.* **2013**, *136*, 1132.
(9) (a) Ackermann, L.; Mulzer, M. *Org. Lett.* **2008**, *10*, 5043. (b) Ackermann, L.; Novák, P. *Org. Lett.* **2009**, *11*, 4966. (c) Ackermann, L.; Hofmann, N.; Vicente, R. *Org. Lett.* **2011**, *13*, 1875. (d) Ackermann, L.; Fenner, S. *Org. Lett.* **2011**, *13*, 6548. (e) Ackermann, L.; Wang, L.; Lygin, A. V. *Chem. Sci.* **2012**, *3*, 177. (f) Ackermann, L.; Pospech, J.; Potukuchi, H. K. *Org. Lett.* **2012**, *14*, 2146. (g) Thirunavukkarasu, V. S.; Hubrich, J.; Ackermann, L. *Org. Lett.* **2012**, *14*, 4210. (h) Ackermann, L.; Vicente, R.; Althammer, A. *Org. Lett.* **2008**, *10*, 2299. (i) Ackermann, L.; Novák, P.; Vicente, R.; Hofmann, N. *Angew. Chem., Int. Ed.* **2009**, *48*, 6045.
(10) (a) Arockiam, P. B.; Fischmeister, C.; Bruneau, C.; Dixneuf, P. H. *Angew. Chem., Int. Ed.* **2010**, *49*, 6629. (b) Li, B.; Devaraj, K.; Darcel, C.; Dixneuf, P. H. *Tetrahedron* **2012**, *68*, 5179. (c) Ferrer Flegeau, E.; Bruneau, C.; Dixneuf, P. H.; Jutand, A. *J. Am. Chem. Soc.* **2011**, *133*, 10161. (d) Arockiam, P.; Poirier, V.; Fischmeister, C.; Bruneau, C.; Dixneuf, P. H. *Green Chem.* **2009**, *11*, 1871.
(11) (a) Dastbaravardeh, N.; Schnürch, M.; Mihovilovic, M. D. *Org. Lett.* **2012**, *14*, 3792. (b) Bergman, S. D.; Storr, T. E.; Prokopcová, H.; Aelvoet, K.; Diels, G.; Meerpoel, L.; Maes, B. U. W. *Chem.—Eur. J.* **2012**, *18*, 10393. (c) Štefane, B.; Fabris, J.; Požgan, F. *Eur. J. Org. Chem.* **2011**, *2011*, 3474.
(12) (a) Ackermann, L.; Althammer, A.; Born, R. *Synlett* **2007**, 2833. (b) Ackermann, L.; Althammer, A.; Born, R. *Tetrahedron* **2008**, *64*, 6115.
(13) Ackermann, L.; Lygin, A. V. *Org. Lett.* **2011**, *13*, 3332.
(14) Du, B.; Jiang, X.; Sun, P. *J. Org. Chem.* **2013**, *78*, 2786.
(15) Caron, L.; Campeau, L.-C.; Fagnou, K. *Org. Lett.* **2008**, *10*, 4533.
(16) Ackermann, L.; Vicente, R. n.; Potukuchi, H. K.; Pirovano, V. *Org. Lett.* **2010**, *12*, 5032.
(17) Bedford, R. B.; Betham, M. *J. Org. Chem.* **2006**, *71*, 9403.
(18) (a) Cuesta, L.; Soler, T.; Urriolabeitia, E. P. *Chem.—Eur. J.* **2012**, *18*, 15178. (b) Butschke, B.; Schwarz, H. *Chem. Sci.* **2012**, *3*, 308.
(19) (a) Albers, M. O.; Singleton, E.; Yates, J. E.; Mccormick, F. B. *Inorg. Synth.* **1989**, *26*, 249. (b) Bennett, M. A.; Huang, T.-N.; Matheson, T. W.; Smith, A. K. *Inorg. Synth.* **1982**, *21*, 74. (c) Hallman, P. S.; Stephenson, T. A.; Wilkinson, G. *Inorg. Synth.* **1970**, *12*, 237.
(20) (a) Tan, C.; Lai, S.; Wu, S.; Hu, S.; Zhou, L.; Chen, Y.; Wang, M.; Zhu, Y.; Lian, W.; Peng, W.; Ji, L.; Xu, A. *J. Med. Chem.* **2010**, *53*, 7613. (b) Kulkarni, A.; Abid, M.; Török, B.; Huang, X. *Tetrahedron Lett.* **2009**, *50*, 1791.
(21) Ho, B. T.; McIsaac, W. M.; Tansey, L. W.; Walker, K. E. *Can. J. Chem.* **1967**, *45*, 2963.
(22) (a) Li, B.; Roisnel, T.; Darcel, C.; Dixneuf, P. H. *Dalton Trans.* **2012**, *41*, 10934. (b) Yellol, G. S.; Donaire, A.; Yellol, J. G.; Vasylyeva, V.; Janiak, C.; Ruiz, J. *Chem. Commun.* **2013**, *49*, 11533.

DOI: 10.1021/acs.joc.5b00411
J. Org. Chem. 2015, 80, 5532−5545