Tetrahedron 69 (2013) 6519–6526

Contents lists available at SciVerse ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Pd(II)-catalyzed C(sp^2)–H carbonylation of biaryl-2-amine: synthesis of phenanthridinones

Zunjun Liang [a], Jitan Zhang [a], Zhanxiang Liu [a], Kai Wang [a], Yuhong Zhang [a,b,*]

[a] Department of Chemistry, ZJU-NHU United R&D Center, Zhejiang University, Hangzhou 310027, China
[b] State Key Laboratory of Applied Organic Chemistry, Lanzhou University, Lanzhou 730000, China

ARTICLE INFO

Article history:
Received 1 March 2013
Received in revised form 26 April 2013
Accepted 10 May 2013
Available online 16 May 2013

Keywords:
Carbonylation
Phenanthridinone
Palladium-catalyzed
Free-amine
C–H activation

ABSTRACT

A $Pd(OAc)_2$-catalyzed C(sp^2)–H carbonylation protocol of arenes under carbon monoxide atmosphere has been developed. The scope of the carbonylation reaction is broad and tolerates a variety of useful functional groups. This reaction provides a novel and efficient method for the synthesis of biologically and pharmaceutically significant phenanthridinones.

1. Introduction

Carbonylation processes using carbon monoxide (CO) as a C_1 building block have proven to be powerful tool to construct important scaffolds in natural products, pharmaceuticals, agrochemicals, and functional materials.[1] Over the past few decades, extensive efforts have been made to develop transition-metal-catalyzed carbonylation of organic halides[2] or organic pseudohalides[3] for the syntheses of carboxylic acids, esters, amides, and so on. From atom-economic and environmentally benign points of view, an attractive alternative to this approach is the development of methods for direct C–H carbonylation reactions.[4] In recent years, carbonylation reactions of C–H bond have been extensively studied under palladium, ruthenium, or rhodium catalysis assisted by directing groups (DGs), such as pyridines,[5] amides,[6] pyridin-2-ylmethylamine moieties,[7] alkyl amines,[8] hydroxyl groups,[9] carboxylic acids,[10] and so on.[11] The combination of C–H carbonylation with a subsequent intramolecular cyclization has allowed efficient access to different heterocycles.[12] Although great achievements have been made, development of highly efficient and atom-economic methods toward other significant targets would be also highly desirable.

Phenanthridinone possess a widespread occurrence as scaffold in a wide variety of compounds with pharmacological properties and biological activities.[13] For example, **PJ34** is a highly selective PARP-1 inhibitors.[14] There are a number of methods for the preparation of 6(5*H*)-phenanthridinones[15] and one of the conventional approaches is through the treatment of fluorenone with NaN_3 in concentrated sulfuric acid, which leads to big environment problem.[16] Based on the direct carbonylation strategy, Zhou and coworkers developed $Pd(OAc)_2$-catalyzed carbonylation of organoboron reagent with CO for the synthesis of phenanthridinones in acetic acid (Fig. 1, Eq. 1).[17] Later, Alper and Lu reported an efficient method for the synthesis of phenanthridinone by intramolecular carbonylation reaction of aryl iodide by palladium catalysis (Fig. 1, Eq. 1).[18] In 2007, Albert successfully applied selective carbonylation of C(sp^2)–H bond for the preparation of phenanthridinones by the use of stoichiometric amount of palladium complex (Fig. 1, Eq. 2).[19] However, these methods require the prefunctionalization of biaryl-2 amine to their halide or metallic derivatives, which are not atom-economic and environmentally benign processes. Our continuous interest in transition-metal-catalyzed C–H bond activation prompted us to explore the novel carbonylation of biphenylamine for the economic preparation of phenanthridinones.[20] Herein, we report a direct carbonylation of C(sp^2)–H for synthesis of phenanthridinones with high efficiency under the mild reaction conditions by the use of 3 mol% $Pd(OAc)_2$ as catalyst and Cu(II) trifluoroacetate as oxidant in trifluoroethanol (Fig. 1, Eq. 3).

* Corresponding author. Tel.: +86 571 8795 2723; fax: +86 571 8795 3244; e-mail address: yhzhang@zju.edu.cn (Y. Zhang).

0040-4020/$ – see front matter © 2013 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.tet.2013.05.025

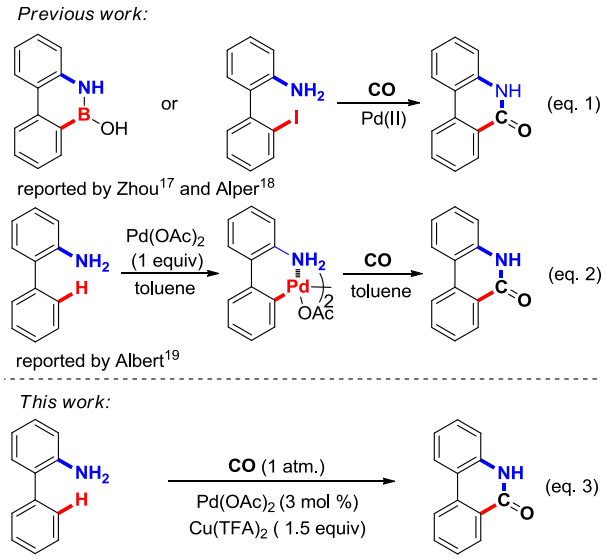


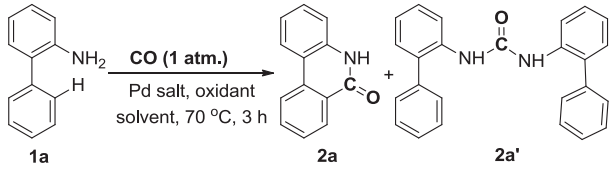
Fig. 1. The synthesis of phenanthridinone.

2. Results and discussion

Initially, we chose biphenyl-2-amine **1a** as a model substrate for the studies of the direct carbonylation (Table 1). CO gas was delivered from a toy balloon at an atmospheric pressure. Gratifyingly, we obtained the desired direct carbonylation product of C(sp^2)–H bond **2a** in 6% yield by the use of 3 mol % $Pd(OAc)_2$ and 1.5 equiv $Cu(OAc)_2$ at 70 °C in trifluoroethanol (TFEtOH), while the aryl urea **2a′** was obtained in 25% yield (Table 1, entry 1). Further copper oxidant screen led to a fruitful results: the yield of **2a** increased to 24% by the use of $CuSO_4$ (Table 1, entry 2), which was further promoted to 54% by the use of $Cu(OTf)_2$ (Table 1, entry 3). The best result was obtained with Cu(II) trifluoroacetate ($Cu(TFA)_2$), to give **2a** in 86% isolated yield (Table 1, entry 4), and only small amounts of urea byproduct **2a′** were observed. Other copper salts, such as $CuCO_3{\cdot}Cu(OH)_2$ and CuO, were found to be ineffective (Table 1, entries 5 and 6). Palladium catalysts, including $Pd(TFA)_2$ and $Pd(dba)_2$, also worked under the reaction conditions, but delivered lower yields (Table 1, entries 7, 8). $PdCl_2$ was almost inactive (Table 1, entry 9). The reaction did not proceed in the absence of palladium catalysts or copper oxidants (Table 1, entries 10, 11). TFEtOH is the best solvent for this transformation (Table 1, entries 12–16). Further investigation[21] of reaction temperature led us to establish the optimized reaction conditions as follows: treatment of biphenyl-2-amine with carbon monoxide (1 atm) in the presence of 3 mol % of $Pd(OAc)_2$ and $Cu(TFA)_2$ (1.5 equiv) in trifluoroethanol at 70 °C. During the preparation of this paper, Zhu and co-workers reported a similar aminocarbonylation of *o*-arylanilines by the use of $Pd(MeCN)_2Cl_2$ as catalyst and $Cu(TFA)_2$ as oxidant in the presence of 1.0 equiv of trifluoroacetic acid.[22]

Once the optimized reaction conditions had been established, we explored the substrate scope of the direct carbonylation as summarized in Table 2. Several structural modifications on the

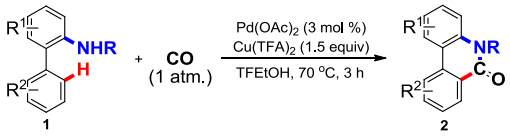
Table 1
Optimization of reaction conditions[a]



Entry	Catalyst	Oxidant	Solvent	Yield (%)[b]
1	$Pd(OAc)_2$	$Cu(OAc)_2$	TFEtOH	6 (25)
2	$Pd(OAc)_2$	$CuSO_4$	TFEtOH	23 (24)
3	$Pd(OAc)_2$	$Cu(OTf)_2$	TFEtOH	54 (0)
4	$Pd(OAc)_2$	$Cu(TFA)_2$	TFEtOH	86 (tr)
5	$Pd(OAc)_2$	$CuCO_3{\cdot}Cu(OH)_2$	TFEtOH	tr (19)
6	$Pd(OAc)_2$	CuO	TFEtOH	tr (21)
7	$Pd(TFA)_2$	$Cu(TFA)_2$	TFEtOH	82 (tr)
8	$Pd(dba)_2$	$Cu(TFA)_2$	TFEtOH	52 (tr)
9	$PdCl_2$	$Cu(TFA)_2$	TFEtOH	tr (tr)
10	$Pd(OAc)_2$	/	TFEtOH	0 (16)
11	/	$Cu(TFA)_2$	TFEtOH	0 (0)
12	$Pd(OAc)_2$	$Cu(TFA)_2$	EtOH	20 (13)
13	$Pd(OAc)_2$	$Cu(TFA)_2$	DMSO	14 (25)
14	$Pd(OAc)_2$	$Cu(TFA)_2$	Toluene	37 (60)
15	$Pd(OAc)_2$	$Cu(TFA)_2$	DCE	62 (34)
16	$Pd(OAc)_2$	$Cu(TFA)_2$	THF	50 (38)

[a] Reaction conditions: **1a** (0.5 mmol), Pd catalyst (0.015 mmol, 3 mol %), oxidant (0.75 mmol, the amount of $Cu(TFA)_2$ based on anhydrate), solvent (1 mL), 70 °C, 3 h.
[b] Isolated yield based on biphenylamine **1a**, the isolated yield of **2a′** is in the parentheses.

Table 2
Carbonylation of biphenyl-2-amine derivatives[a]



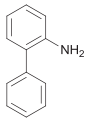
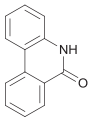
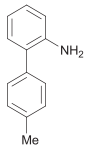
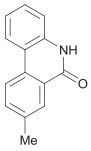
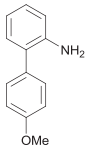
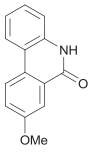
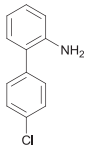
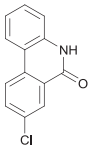
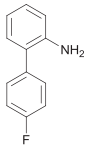
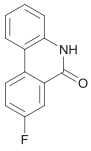
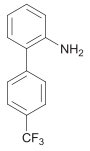
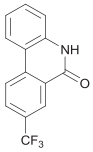
Entry	Substrate **1**	Product **2**	Yield (%)[b]
1	 **1a**	 **2a**	86
2	 **1b**	 **2b**	81
3	 **1c**	 **2c**	84
4	 **1d**	 **2d**	57
5	 **1e**	 **2e**	63
6	 **1f**	 **2f**	55

Table 2 (*continued*)

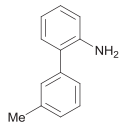
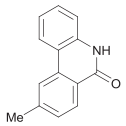
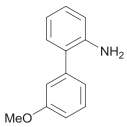
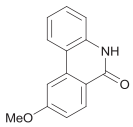
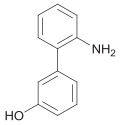
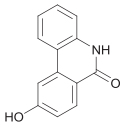
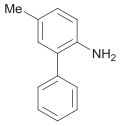
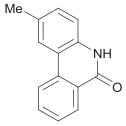
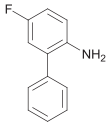
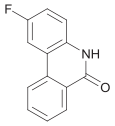
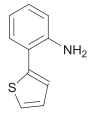
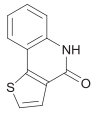
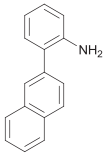
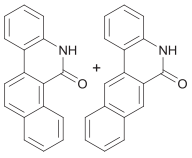
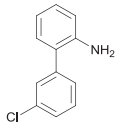
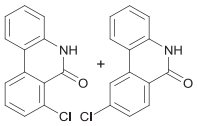
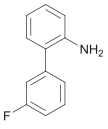
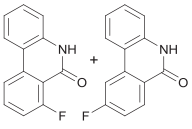
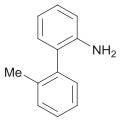
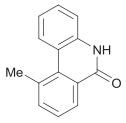
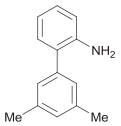
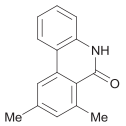
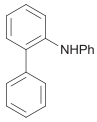
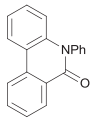
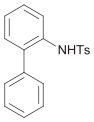
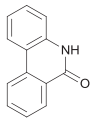
Entry	Substrate **1**	Product **2**	Yield (%)[b]
7	 **1g**	 **2g**	94
8	 **1h**	 **2h**	95
9	 **1i**	 **2i**	65
10	 **1j**	 **2j**	96
11	 **1k**	 **2k**	80
12	 **1l**	 **2l**	65
13	 **1m**	 **2m:2m'** = 1:1	52
14	 **1n**	 **2n:2n'** = 1:9	51
15	 **1o**	 **2o:2o'** = 2:5	65
16	 **1p**	 **2p**	57

Table 2 (*continued*)

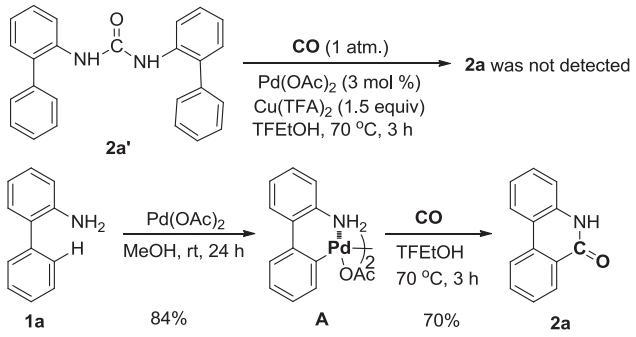
Entry	Substrate **1**	Product **2**	Yield (%)[b]
17	 **1q**	 **2q**	0
18	 **1r**	 **2r**	52
19	 **1s**	 **2a**	30

[a] Reaction conditions: **1** (0.5 mmol), $Pd(OAc)_2$ (0.015 mmol), $Cu(TFA)_2$ (217 mg, 1.5 equiv), TFEtOH (1.0 mL), 70 °C, 3 h.
[b] Isolated yields based on biphenylamine **1**.

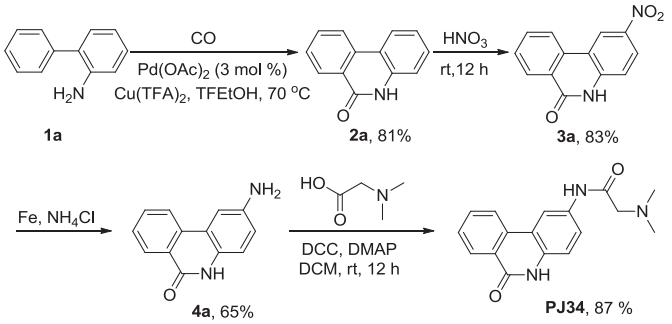
biphenyl moiety were introduced, including methyl (Table 2, entries 2, 7, and 10), methoxy (Table 2, entries 3 and 8), chloride.

(Table 2, entry 4), fluoride (Table 2, entry 5), and trifluoromethyl (Table 2, entry 6). Noteworthy, the hydroxyl group was tolerated under the reaction conditions and phenanthridinone **2i** was obtained in 65% yield (Table 2, entry 9). The electronic properties of substituent groups have a significant effect on the reaction. It was found that electron-rich biphenylamines (Table 2, entries 1–3, 7, 8, and 10) exhibited better reactivity and gave higher yields than those of the electron-deficient biphenylamines (Table 2, entries 4–6 and 11). It is noteworthy that the carbonylation reaction was compatible with aromatic heterocycle to deliver the desired product in moderate yield (Table 2, entry 12). 2-(Naphthalen-2-yl)aniline underwent the carbonylation reaction smoothly to give the two isomers (**2m**:**2m′**, detected by ^{1}H NMR) in 1:1 M ratio (Table 2, entry 13). The steric hindrance played a role in this transformation. The *meta*-position substituted substrates gave the major products with the carbonylation at the less hindered *ortho* position (**2n**/**2n′** and **2o**/**2o′**; Table 2, entries 14 and 15). In addition, 2′-methyl substrate **1p** showed a lower efficiency to give the product **2p** in 57% yield (Table 2, entry 16). When 3′,5′-dimethyl substrate (**1q**) was used, the desired product was not observed (Table 2, entry 17). To our delight, *N*-aryl protected biphenyl-2-amine **1r** tolerated the carbonylation reaction conditions and generated the corresponding *N*-phenyl 6(5*H*)-phenanthridinones **2r** in moderate yield (Table 2, entry 18). Surprisingly, only detosylation product was detected when *N*-Ts substituted biphenyl-2-amine was subjected into the reaction (Table 2, entry 19).[23]

In our experiments, traces of aryl ureas as byproducts were always observed. We performed the reaction of 1-(biphenyl-2-yl)-3-(biphenyl-2-ylmethyl)urea **2a′** with carbon monoxide under standard reaction conditions (Scheme 1), and the desired phenanthridinone **2a** was not found, illustrating that the product **2a** was not transformed from urea **2a′**. To obtain more information about the reaction mechanism, the palladacycle complex **A** was synthesized by a method previously described in the literature.[19,24] Treatment of the palladacycle complex **A** with carbon monoxide in the absence of copper oxidant indeed afforded the desired product **2a** in 70% yield (Scheme 1). These results indicate that the free-amine group works as the directing group and palladacycle complex **A** may be the key reactive intermediate in this C(sp^2)–H activation process.



Scheme 1. Mechanism studies on the carbonylation reaction.



Scheme 2. The synthesis of **PJ34**.

A plausible reaction mechanism has been proposed based on the experiment results and the chemistry of C–H bond activation (Fig. 2).[25] First, free-amine assisted palladation of C(sp^2)–H bond occurs to form the key six-membered palladacycle intermediate **A**, followed by the coordination of CO to give the intermediate **B**. The subsequent insertion of C–Pd bond to CO leads to the formation of intermediate **C**. A proton of amine (NH_2) abstraction may take place to give intermediate **D**, which undergoes the reductive elimination to afford the final product **2a**. The direct carbonylation of amine (NH_2) leads to the formation of the urea byproduct,[26] which can be suppressed in our experiment by the suitable choice of copper oxidant. The formed Pd(0) is oxidized to Pd(II) by Cu(II) salts in the system to fulfill the catalytic cycle.

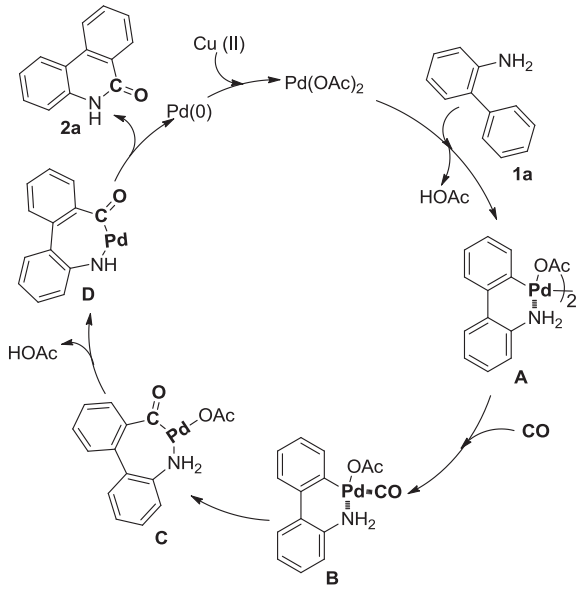


Fig. 2. A plausible mechanism.

To illustrate the suitability of this methodology, the known bioactive molecules Phenaglydon (**2g**)[27] and **PJ34** were synthesized (Scheme 2). Phenaglydon (**2g**) can be obtained in 94% yield in one step (Table 2). Phenanthridin-6(5*H*)-one (**2a**), precursor of **PJ34**, can be obtained in 81% yield up to a 5 mmol level scale. The bioactive phenanthridinone **PJ34** was synthesized from **2a** by consecutive nitration, reduction, and amidation in 38% overall yield.[28]

3. Conclusions

In summary, we have developed a novel protocol for free-amine directed carbonylation of C(sp^2)–H by palladium catalysis. Various substituents of biphenylamines were tolerated under the standard conditions. This transformation provided an efficient method for the synthesis of biologically important phenanthridinones. Detailed mechanistic studies of this carbonylation reaction and application of this catalysis to other substrates are ongoing in our laboratory.

4. Experimental section

4.1. General experimental methods

The materials and solvents were purchased from common commercial sources and used without additional purification, if there is no special version. NMR spectra were recorded for ^{1}H NMR at 400 MHz or 500 MHz, and ^{13}C NMR at 100 MHz or 125 MHz using TMS as internal standard. The following abbreviations were used to describe peak patterns were appropriate: singlet (s), doublet (d), triplet (t), multiplet (m), doublet of doublet (dd), broad resonances (br). Mass spectroscopy data of the products were collected on an HRMS-APCI instrument or a low-resolution MS instrument using EI or ESI ionization. Infrared spectra were recorded on an FTIR spectrometer.

4.2. General procedure for preparation of biphenylamine derivatives[29]

A vessel with a magnetic stir bar was charged with Na_2CO_3 (2.120 g, 20 mmol, 2.0 equiv), $Pd(OAc)_2$ (112 mg, 0.500 mmol, 5 mol %), 2-bromoaniline (10 mmol, 1.0 equiv), arylboronic acid (15 mmol, 1.5 equiv), distilled water (35 mL), and acetone (30 mL). Then the mixture was stirred for 12 h at 35 °C. Afterward the resulting solution was filtered through a plug of Celite and the residue was washed with ethyl acetate (30 mL). The filtrate was extracted three times with diethyl ether (3×30 mL). The combined organic phases were washed with brine (40 mL), dried over anhydrous sodium sulfate, filtered, and concentrated. The residue was purified by flash column chromatography with ethyl acetate (EA) and petroleum ether (Pet) as eluent to afford the corresponding 2-amidobiphenyl derivatives (**1b**–**1k**, **1m**–**1o**, and **1q**).

*4.2.1. 4′-Methylbiphenyl-2-amine (**1b**).* ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 7.34 (d, 2H, J=8.0 Hz), 7.25 (t, 2H, J=4.0 Hz), 7.11–7.16 (m, 2H), 6.76–6.84 (m, 2H), 3.75 (br s, 2H), 2.39 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$, TMS) δ 143.5, 136.8, 136.5, 130.4, 129.5, 128.9, 128.3, 127.6, 118.6, 115.6, 21.2.

*4.2.2. 4′-Methoxybiphenyl-2-amine (**1c**).* ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 7.37 (d, J=6.4 Hz, 2H), 7.09–7.12 (m, 2H), 6.97 (d, J=6.8 Hz, 2H), 6.80 (t, J=7.0 Hz, 1H), 6.74 (d, J=8.4 Hz, 1H), 3.83 (s, 3H), 3.60 (br s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$, TMS) δ 158.8, 143.6, 131.8, 130.5, 130.2, 128.2, 127.4, 118.7, 115.6, 114.3, 55.4.

*4.2.3. 4′-Chlorobiphenyl-2-amine (**1d**).* ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 7.38–7.42 (m, 4H), 7.16 (t, 1H, J=7.6 Hz), 7.08 (d, J=7.2 Hz,

1H), 6.82 (t, *J*=7.6 Hz, 1H), 6.75 (d, *J*=7.6 Hz, 1H), 3.70 (br s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$, TMS) δ 143.4, 137.9, 133.1, 130.5, 130.3, 129.0, 128.8, 126.3, 118.8, 115.7.

*4.2.4. 4′-Fluorobiphenyl-2-amine (**1e**).* ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 7.39–7.43 (m, 2H), 7.07–7.17 (m, 4H), 6.81 (t, *J*=7.6 Hz, 1H), 6.75 (d, *J*=8.0 Hz, 1H), 3.64 (br s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$, TMS) δ 162.1 (d, *J*=244.8 Hz), 143.5, 135.4 (d, *J*=3.6 Hz), 130.8 (d, *J*=7.9 Hz), 130.5, 128.7, 126.7, 118.8, 115.8 (d, *J*=11.3 Hz), 115.7.

*4.2.5. 4′-(Trifluoromethyl)biphenyl-2-amine (**1f**).* ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 7.69 (d, *J*=8.0 Hz, 2H), 7.57 (d, *J*=7.6 Hz, 2H), 7.18 (t, *J*=7.6 Hz, 1H), 7.10 (d, *J*=7.6 Hz, 1H), 6.84 (t, *J*=7.6 Hz, 1H), 6.76 (d, *J*=8.0 Hz, 1H), 3.73 (br s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS) δ 143.4, 132.6, 130.4, 129.5, 129.3, 128.4, 126.1, 125.8 (q, *J*=3.8 Hz), 124.3 (q, *J*=270.3 Hz), 118.9, 116.0.

*4.2.6. 3′-Methylbiphenyl-2-amine (**1g**).* ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 7.33 (t, *J*=7.2 Hz, 1H), 7.24–7.26 (m, 2H), 7.11–7.16 (m, 3H), 6.81 (t, *J*=7.6 Hz, 1H), 6.76 (d, *J*=7.6 Hz, 1H), 3.68 (br s, 2H), 3.39 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$, TMS) δ 143.0, 139.4, 138.5, 130.5, 129.9, 128.7, 128.4, 128.1, 128.0, 126.1, 119.0, 115.9, 21.5.

*4.2.7. 3′-Methoxybiphenyl-2-amine (**1h**).* ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 7.35 (t, *J*=8.0 Hz, 1H), 7.12–7.17 (m, 2H), 7.03 (d, *J*=7.2 Hz, 1H), 6.99 (s, 1H), 6.89 (d, *J*=8.0 Hz, 1H), 6.81 (t, *J*=7.6 Hz, 1H), 6.76 (d, *J*=8.0 Hz, 1H), 3.83 (s, 3H), 3.66 (br s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$, TMS) δ 159.9, 143.1, 140.9, 130.4, 129.9, 128.6, 127.7, 121.4, 118.9, 115.8, 114.5, 113.0, 55.3.

*4.2.8. 2′-Aminobiphenyl-3-ol (**1i**).* ^{1}H NMR (400 MHz, CD_3SOCD_3, TMS) δ 9.47 (br s, 1H), 7.24 (t, *J*=8.2 Hz, 1H), 7.03 (t, *J*=7.8 Hz, 1H), 6.96 (d, *J*=7.2 Hz, 1H), 6.81–6.82 (m, 2H), 6.73–6.74 (m, 2H), 6.62 (t, *J*=7.4 Hz, 1H), 4.68 (br s, 2H); ^{13}C NMR (100 MHz, CD_3SOCD_3, TMS) δ 157.8, 145.1, 141.3, 130.1, 130.1, 128.4, 126.2, 119.6, 117.1, 115.7, 115.5, 114.1.

*4.2.9. 5-Methylbiphenyl-2-amine (**1j**).* ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 7.41–7.46 (m, 4H), 7.31–7.35 (m, 1H), 6.96–6.99 (m, 2H), 6.70 (d, *J*=8.0 Hz, 1H), 3.54 (br s, 2H), 2.28 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$, TMS) δ 141.0, 139.7, 131.0, 129.1, 129.0, 128.8, 127.9, 127.8, 127.1, 115.9, 20.5.

*4.2.10. 5-Fluorobiphenyl-2-amine (**1k**).* ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 7.43–7.46 (m, 4H), 7.36–7.37 (m, 1H), 6.85–6.87 (m, 2H), 6.67–6.70 (m, 1H), 3.60 (br s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS) δ 156.3 (d, *J*=235.5 Hz), 139.4, 138.4, 128.9, 128.8, 128.6 (d, *J*=7.7 Hz), 127.5, 116.6 (d, *J*=28.6 Hz), 116.5, 114.8 (d, *J*=22.1 Hz).

*4.2.11. 2-(Naphthalen-2-yl)aniline (**1m**).* ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 7.85–7.93 (m, 4H), 7.59 (d, *J*=8.8 Hz, 1H), 7.19–7.52 (m, 2H), 7.18–7.22 (m, 2H), 6.87 (t, *J*=7.6 Hz, 1H), 6.81 (d, *J*=8.0 Hz, 1H), 3.88 (br s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$, TMS) δ 143.7, 137.0, 133.7, 132.5, 130.7, 128.7, 128.5, 128.0, 127.9, 127.8, 127.6, 127.5, 126.4, 126.1, 118.8, 115.8.

*4.2.12. 3′-Chlorobiphenyl-2-amine (**1n**).* ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 7.46 (s, 1H), 7.31–7.39 (m, 3H), 7.16 (t, *J*=7.6 Hz, 1H), 7.09 (d, *J*=7.6 Hz, 1H), 6.83 (t, *J*=7.4 Hz, 1H), 6.76 (d, *J*=8.0 Hz, 1H), 3.74 (br s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$, TMS) δ 143.2, 141.3, 134.7, 130.4, 130.1, 129.2, 129.0, 127.4, 127.3, 126.3, 118.9, 115.9.

*4.2.13. 3′-Fluorobiphenyl-2-amine (**1o**).* ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 7.36–7.42 (m, 1H), 7.22–7.24 (m, 1H), 7.14–7.18 (m, 2H), 7.10 (d, *J*=7.2 Hz, 1H), 7.01–7.05 (m, 1H), 6.82 (t, *J*=7.74 Hz, 1H), 6.76 (d, *J*=7.6 Hz, 1H), 3.64 (br s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$, TMS) δ 163.0 (d, *J*=244.0 Hz), 143.3, 141.7 (d, *J*=7.8 Hz), 130.3 (d, *J*=8.4 Hz), 130.3, 128.9, 126.3, 124.8 (d, *J*=3.8 Hz), 118.8, 116.1 (d, *J*=21.3 Hz), 115.8, 114.1 (d, *J*=21.1 Hz).

*4.2.14. 3′,5′-Dimethylbiphenyl-2-amine (**1q**).* ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 7.19–7.21 (m, 2H), 7.15 (s, 2H), 7.07 (s, 1H), 6.89 (t, *J*=7.4 Hz, 1H), 6.82 (d, *J*=8.0 Hz, 1H), 3.79 (br s, 2H), 2.45 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS) δ 143.5, 139.4, 138.3, 130.3, 128.7, 128.2, 127.9, 126.8, 118.5, 115.5, 21.3.

*4.2.15. 2-(Thiophen-2-yl)aniline (**1l**).*[30] To a dry round bottom flask, equipped with a magnetic stir bar, thiophen-2-ylboronic acid (7.5 mmol, 1.5 equiv), K_2CO_3 (2.760 g, 20 mmol, 4.0 equiv), and $PdCl_2(PPh_3)_2$ (344 mg, 0.500 mmol, 10 mol %) were dissolved in 50 mL of DMF and 10 mL of H_2O (DMF:H_2O=5:1). 2-Bromoaniline (860 mg, 5.0 mmol, 1.0 equiv) was added, and the resulting mixture was heated to 80 °C and stirring for 24 h. After cooling to room temperature, the reaction mixture was poured into water, and then the product was extracted with CH_2Cl_2 (3×30 mL), washed with brine (40 mL), dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel to give 2-(thiophen-2-yl) aniline (**1l**). ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 7.33 (d, *J*=5.2 Hz, 1H), 7.27 (d, *J*=7.6 Hz, 1H), 7.19 (d, *J*=3.2 Hz, 1H), 7.10–7.16 (m, 2H), 6.75–6.80 (m, 2H), 3.94 (br s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$, TMS) δ 144.1, 141.1, 131.0, 129.1, 127.6, 125.8, 125.3, 120.0, 118.6, 115.9.

*4.2.16. 2′-Methylbiphenyl-2-amine (**1p**).*[31] To a 100 mL round bottom flask equipped with a magnetic stir bar, *o*-tolylboronic acid (15 mmol, 1.5 equiv), K_2CO_3 (5.520 g, 40 mmol, 4.0 equiv), and $Pd(PPh_3)_4$ (1154 mg, 1.000 mmol, 0.1 equiv) were dissolved in 45 mL toluene followed by the addition of 9 mL of H_2O and 15 mL of EtOH. Then 2-bromoaniline (10 mmol, 1.0 equiv) was added and the resulting mixture was stirred at 100 °C for 16 h. After cooling to room temperature, the biphasic solution was diluted with 50 mL of saturated aqueous NH_4Cl, and 30 mL of CH_2Cl_2. The aqueous phase was extracted with diethyl ether (3×30 mL) and the combined organic layers were washed with brine (40 mL), dried over anhydrous sodium sulfate, filtered, and concentrated. The residue was purified by flash column chromatography with ethyl acetate (EA) and petroleum ether (Pet) as eluent to afford the corresponding 2′-methylbiphenyl-2-amine (**1p**). ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 7.16–7.28 (m, 5H), 7.01 (d, *J*=7.2 Hz, 1H), 6.80 (t, *J*=7.4 Hz, 1H), 6.76 (d, *J*=7.6 Hz, 1H), 3.44 (br s, 2H), 2.17 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS) δ 143.5, 138.6, 136.9, 130.2, 130.0, 130.0, 128.3, 127.7, 127.4, 126.1, 118.2, 115.0, 19.6.

*4.2.17. N-Phenyl-[1,1′-biphenyl]-2-amine (**1r**).* To a 50 mL round bottom flask equipped with a magnetic stir bar, biphenyl-2-amine **1a** (1.69 g, 10 mmol, 1.0 equiv), boronic acid (30 mmol, 3.0 equiv), $Pd(OAc)_2$ (112 g, 0.5 mmol, 0.05 equiv), $Cu(OAc)_2 \cdot H_2O$ (1.99 g, 10 mmol, 1.0 equiv), and HOAc (20 mmol) were dissolved in 30 mL of trifluoroethanol and the resulting mixture was stirred at 90 °C for 20 h. After cooling to room temperature, 50 mL of saturated aqueous Na_2CO_3, and 30 mL of ethyl acetate were added and the organic layer was collected. The aqueous phase was extracted with ethyl acetate (3×20 mL). The combined organic phases were washed with brine (40 mL), dried over anhydrous sodium sulfate, filtered, and concentrated. The residue was purified by flash column chromatography with ethyl acetate (EA) and petroleum ether (Pet) as eluent to afford the corresponding products **1r**. ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 7.32–7.45 (m, 6H), 7.22–7.26 (m, 4H), 6.97–7.04 (m, 3H), 6.91 (t, *J*=7.4 Hz, 1H), 5.41 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS) δ 143.4, 140.2, 139.1, 131.6, 131.0, 129.4, 129.4, 129.0, 128.3, 127.5, 121.1, 121.1, 118.3, 117.5.

*4.2.18. N-([1,1′-Biphenyl]-2-yl)-4-methylbenzenesulfonamide (**1s**).* Methylbenzene-1-sulfonyl chloride (2.85 g, 15 mmol, 1.5 equiv) in

20 mL of THF was added dropwise to the mixture of biphenyl-2-amine **1a** (1.69 g, 10 mmol, 1.0 equiv), Et_3N (10 mL), and THF (15 mL) at room temperature in 30 min. The result mixture was heated to 60 °C and stirred until completion of the reaction. After cooling to room temperature, 50 mL of saturated aqueous Na_2CO_3, and 30 mL of ethyl acetate were added and the organic layer was collected. The aqueous phase was extracted with ethyl acetate (3×20 mL). The combined organic phases were washed with brine (40 mL), dried over anhydrous sodium sulfate, filtered, and concentrated. The residue was purified by flash column chromatography with ethyl acetate (EA) and petroleum ether (Pet) as eluent to afford the corresponding products **1s**. ^{1}H NMR (400 MHz, CDCl3, TMS) δ 7.71 (dd, *J*=8.0, 0.8 Hz, 1H), 7.46 (d, *J*=8.4 Hz, 2H), 7.30–7.36 (m, 4H), 7.18 (d, *J*=8.4 Hz, 2H), 7.08–7.16 (m, 2H), 6.84–6.86 (m, 2H), 6.58 (s, 1H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, CDCl3, TMS) δ 143.9, 137.2, 136.2, 134.0, 133.8, 130.3, 129.6, 129.1, 128.9, 128.7, 128.1, 127.2, 124.9, 121.4, 21.6.

4.3. General procedure for carbonylation of biphenylamines

$Pd(OAc)_2$ (3 mg, 0.015 mmol), $Cu(TFA)_2 \cdot xH_2O$ (217 mg, 0.75 mmol), biphenylamine (0.5 mmol), and trifluoroethanol (1.0 mL) was added to a three-necked flask equipped with a magnetic stirring bar and reflux condenser. Then a toy balloon filled with carbon monoxide gas was connected to the flask. The mixture was stirred for 3 h at 70 °C. After cooled to room temperature, the mixture was filtered through a plug of Celite, and the residue was washed with ethyl acetate (2×20 mL). The filtrate was evaporated in vacuo. The residue was purified by flash column chromatography on silica gel with ethyl acetate (EA) and petroleum ether (Pet) as eluent to afford the corresponding products.

*4.3.1. Phenanthridin-6(5H)-one (**2a**).*[17] 86% yield; ^{1}H NMR (500 MHz, CD_3SOCD_3, TMS) δ 11.71 (br s, 1H miss), 8.52 (d, *J*=8.5 Hz, 1H), 8.40 (d, *J*=7.5 Hz, 1H), 8.35 (dd, *J*=8.0, 1.0 Hz, 1H), 7.85–7.89 (m, 1H), 7.65–7.68 (m, 1H), 7.49–7.53 (m, 1H), 7.39–7.40 (m, 1H), 7.27–7.30 (m, 1H); ^{13}C NMR (125 MHz, CD_3SOCD_3, TMS) δ 160.7, 136.4, 134.2, 132.8, 129.6, 127.9, 127.4, 125.6, 123.2, 122.6, 122.3, 117.5, 116.0; MS (EI) *m*/*z* (%) 195 (100) [M^+], 167 (41), 139 (34), 113 (12); IR (KBr plate, cm^{-1}) ν 3468, 3166, 3047, 1663, 1631, 1609, 1470, 1424, 1369, 749, 727.

*4.3.2. 1,3-Di(biphenyl-2-yl)urea (**2a′**, new compound).* White solid; mp 189–190 °C; ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 7.73 (d, *J*=8.0 Hz, 2H), 7.30–7.35 (m, 6H), 7.23–7.26 (m, 2H), 7.19–7.21 (m, 6H), 7.12–7.141 (m, 2H), 6.38 (br s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$, TMS) δ 153.3, 138.2, 134.7, 134.1, 130.3, 129.1, 128.9, 128.6, 127.7, 124.6, 122.9; HRMS (EI) calcd for $C_{25}H_{20}N_2O$ [M^+] 364.1576; Found, 364.1579; MS (EI) *m*/*z* (%) 364 (19) [M^+], 178 (26), 169 (100), 167 (78), 152 (21), 139 (16), 115 (10); IR (KBr plate, cm^{-1}) ν 3255, 3058, 1622, 1566, 754, 743, 697.

*4.3.3. 8-Methylphenanthridin-6(5H)-one (**2b**).*[32] 81% yield; ^{1}H NMR (500 MHz, CD_3SOCD_3, TMS) δ 11.63 (br s, 1H), 8.39 (d, *J*=8.5 Hz, 1H), 8.34 (d, *J*=8.0 Hz, 1H), 8.14 (s, 1H), 7.68 (dd, *J*=8.0, 1.0 Hz, 1H), 7.46 (t, *J*=7.8 Hz, 1H), 7.36 (d, *J*=8.0 Hz, 1H), 7.25 (t, *J*=7.5 Hz, 1H), 2.49 (s, 3H); ^{13}C NMR (125 MHz, CD_3SOCD_3, TMS) δ 160.8, 137.6, 136.2, 133.9, 131.8, 129.0, 127.2, 125.6, 122.9, 122.6, 122.2, 117.7, 116.0, 20.9; MS (EI) *m*/*z* (%) 209 (100) [M^+], 180 (32), 152 (18), 127 (14); IR (KBr plate, cm^{-1}) ν 3435, 3022, 2890, 1680, 1619, 1486, 1359, 820, 746.

*4.3.4. 8-Methoxyphenanthridin-6(5H)-one (**2c**).*[33] 84% yield; ^{1}H NMR (500 MHz, CD_3SOCD_3, TMS) δ 11.72 (br s, 1H), 8.43 (d, *J*=9.0 Hz, 1H), 8.30 (d, *J*=8.0 Hz, 1H), 7.78 (d, *J*=3.0 Hz, 1H), 7.43–7.46 (m, 2H), 7.37 (d, *J*=7.5 Hz, 1H), 7.23–7.26 (m, 1H), 3.93 (s, 3H); ^{13}C NMR (125 MHz, CD_3SOCD_3, TMS) δ 160.5, 159.0, 135.5, 128.4, 127.6, 127.1, 124.5, 122.6, 122.2, 121.6, 117.7, 115.9, 108.7, 55.4; MS (EI) *m*/*z* (%) 225 (100) [M^+], 210 (16), 195 (12), 182 (21), 154 (49), 127 (22); IR (KBr plate, cm^{-1}) ν 3436, 3026, 2965, 2903, 1666, 1616, 1486, 1367, 1276, 1220, 832, 750.

*4.3.5. 8-Chlorophenanthridin-6(5H)-one (**2d**).*[34] 57% yield; ^{1}H NMR (500 MHz, CD_3SOCD_3, TMS) δ 11.86 (br s, 1H), 8.54 (d, *J*=9.0 Hz, 1H), 8.38 (d, *J*=8.0 Hz, 1H), 8.25 (d, *J*=2.0 Hz, 1H), 7.89 (dd, *J*=8.5, 2.3 Hz, 1H), 7.52 (t, *J*=7.8 Hz, 1H), 7.39 (d, *J*=8.0 Hz, 1H), 7.29 (t, *J*=7.8 Hz, 1H); ^{13}C NMR (125 MHz, CD_3SOCD_3, TMS) δ 159.7, 136.4, 133.1, 132.7, 132.7, 130.0, 127.1, 126.5, 125.1, 123.4, 122.5, 116.8, 116.2; MS (EI) *m*/*z* (%) 229 (100) [M^+], 201 (7), 166 (35), 139 (27); IR (KBr plate, cm^{-1}) ν 3436, 3026, 2889, 1675, 1606, 1468, 741.

*4.3.6. 8-Fluorophenanthridin-6(5H)-one (**2e**).*[33] 63% yield; ^{1}H NMR (500 MHz, CD_3SOCD_3, TMS) δ 11.85 (br s, 1H), 8.58–8.61 (m, 1H), 8.37 (d, *J*=8.0 Hz, 1H), 7.99 (dd, *J*=9.5, 3.0 Hz, 1H), 7.72–7.76 (m, 1H), 7.51 (t, *J*=7.8 Hz, 1H), 7.39 (d, *J*=8.0 Hz, 1H), 7.28 (t, *J*=7.5 Hz, 1H); ^{13}C NMR (125 MHz, CD_3SOCD_3, TMS) δ 161.5 (d, *J*=244.6 Hz), 159.9 (d, *J*=3.1 Hz), 136.0, 131.0 (d, *J*=2.0 Hz), 129.4, 127.6 (d, *J*=7.6 Hz), 125.8 (d, *J*=8.3 Hz), 123.2, 122.5, 120.9 (d, *J*=23.4 Hz), 117.0, 116.2, 112.5 (d, *J*=21.6 Hz); MS (EI) *m*/*z* (%) 213 (100) [M^+], 185 (33), 157 (26), 131 (8); IR (KBr plate, cm^{-1}) ν 3436, 3179, 3033, 2899, 1685, 1677, 1619, 1484, 1362, 817, 748.

*4.3.7. 8-(Trifluoromethyl)phenanthridin-6(5H)-one (**2f**).*[35] 55% yield; ^{1}H NMR (500 MHz, CD_3SOCD_3, TMS) δ 11.97 (br s, 1H miss), 8.73 (d, *J*=8.5 Hz, 1H), 8.56 (s, 1H), 8.46 (d, *J*=8.0 Hz, 1H), 8.15 (dd, *J*=8.5, 1.3 Hz, 1H), 7.59 (t, *J*=7.5 Hz, 1H), 7.41 (d, *J*=8.0 Hz, 1H), 7.32 (t, *J*=7.8 Hz, 1H); ^{13}C NMR (125 MHz, CD_3SOCD_3, TMS) δ 159.9, 137.5, 137.2, 130.9, 128.6 (q, *J*=3.5 Hz), 127.9 (q, *J*=32.3 Hz), 125.8, 124.4 (q, *J*=4.3 Hz), 124.3, 124.0, 123.9 (q, *J*=271.5 Hz), 122.6, 116.5, 116.4; MS (EI) *m*/*z* (%) 263 (100) [M^+], 235 (15), 166 (20), 155 (18), 139 (17), 127 (21); IR (KBr plate, cm^{-1}) ν 3436, 3166, 3030, 2900, 1667, 1623, 1423, 1319, 1271, 1148, 1124, 1104, 828, 751.

*4.3.8. 9-Methylphenanthridin-6(5H)-one (**2g**).*[32] 94% yield; ^{1}H NMR (400 MHz, CD_3SOCD_3, TMS) δ 11.61 (br s, 1H), 8.37 (d, *J*=8.4 Hz, 1H), 8.32 (s, 1H), 8.21 (d, *J*=8.0 Hz, 1H), 7.45–7.50 (m, 2H), 7.35–7.37 (m, 1H), 7.24–7.28 (m, 1H), 2.54 (s, 3H); ^{13}C NMR (125 MHz, CD_3SOCD_3, TMS) δ 160.8, 142.9, 136.7, 134.2, 129.4, 129.1, 127.4, 123.4, 123.1, 122.4, 122.1, 117.5, 116.0, 21.5; MS (EI) *m*/*z* (%) 209 (100) [M^+], 180 (56), 152 (22); IR (KBr plate, cm^{-1}) ν 3438, 3036, 3007, 2917, 1672, 1617, 1366, 751, 671.

*4.3.9. 9-Methoxyphenanthridin-6(5H)-one (**2h**).*[33] 95% yield; ^{1}H NMR (400 MHz, CD_3SOCD_3, TMS) δ 11.63 (br s, 1H), 8.39 (d, *J*=8.5 Hz, 1H), 8.34 (d, *J*=8.0 Hz, 1H), 8.14 (s, 1H), 7.68 (dd, *J*=8.0, 1.0 Hz, 1H), 7.46 (t, *J*=7.8 Hz, 1H), 7.36 (d, *J*=8.0 Hz, 1H), 7.25 (t, *J*=7.5 Hz, 1H), 2.49 (s, 3H); ^{13}C NMR (125 MHz, CD_3SOCD_3, TMS) δ 162.8, 160.6, 137.0, 136.4, 129.6, 129.5, 123.6, 121.9, 119.2, 117.4, 116.2, 116.0, 105.1, 55.8; MS (EI) *m*/*z* (%) 225 (100) [M^+], 196 (8), 182 (26), 154 (41), 127 (22); IR (KBr plate, cm^{-1}) ν 3451, 3140, 2880, 1659, 1608, 1508, 1459, 1428, 1362, 1235, 1221, 1031, 839, 744.

*4.3.10. 9-Hydroxyphenanthridin-6(5H)-one (**2i**).*[36] 65% yield; ^{1}H NMR (400 MHz, CD_3SOCD_3, TMS) δ 11.41 (br s, 1H), 10.47 (br s, 1H), 8.16–8.19 (m, 2H), 7.69 (d, *J*=2.4 Hz, 1H), 7.46 (t, *J*=7.4 Hz, 1H), 7.33 (d, *J*=7.6 Hz, 1H), 7.23 (t, *J*=7.6 Hz, 1H), 7.08 (dd, *J*=8.8, 2.2 Hz, 1H); ^{13}C NMR (125 MHz, CD_3SOCD_3, TMS) δ 161.5, 160.7, 137.0, 136.3, 129.8, 129.4, 123.0, 121.9, 118.0, 117.4, 116.9, 116.0, 106.8; MS (EI) *m*/*z* (%) 211 (100) [M^+], 182 (7), 154 (22), 127 (13); IR (KBr plate, cm^{-1}) ν 3423, 3173, 1653, 1629, 1611, 1446, 1416, 1377, 1241, 749.

*4.3.11. 2-Methylphenanthridin-6(5H)-one (**2j**).*[37] 96% yield; ^{1}H NMR (500 MHz, CD_3SOCD_3, TMS) δ 11.63 (br s, 1H), 8.49 (d, *J*=8.0 Hz, 1H),

8.34 (dd, *J*=8.0, 0.5 Hz, 1H), 8.20 (s, 1H), 7.83–7.86 (m, 1H), 7.64 (t, *J*=7.3 Hz, 1H), 7.28–7.33 (m, 2H), 2.43 (s, 3H); ^{13}C NMR (125 MHz, CD_3SOCD_3, TMS) δ 160.6, 134.4, 134.2, 132.6, 131.2, 130.5, 127.7, 127.4, 125.7, 123.0, 122.5, 117.4, 116.0, 20.7; MS (EI) *m*/*z* (%) 209 (28) [M$^+$], 180 (15), 152 (32), 126 (21), 101 (38), 75 (69), 63 (64), 51 (91), 39 (100); IR (KBr plate, cm^{-1}) ν 3436, 3164, 3018, 2869, 1659, 1609, 1561, 1370, 1153, 772, 650.

*4.3.12. 2-Fluorophenanthridin-6(5H)-one (**2k**).*[37] 80% yield; ^{1}H NMR (500 MHz, CD_3SOCD_3, TMS) δ 11.75 (br s, 1H), 8.52 (d, *J*=8.0 Hz, 1H), 8.35 (dd, *J*=7.5, 0.5 Hz, 1H), 8.27 (dd, *J*=10.0, 1.5 Hz, 1H), 7.86–7.89 (m, 1H), 7.70 (t, *J*=7.5 Hz, 1H), 7.39–7.41 (m, 2H); ^{13}C NMR (125 MHz, CD_3SOCD_3, TMS) δ 160.5, 157.8 (d, *J*=234.6 Hz), 133.5 (d, *J*=2.0 Hz), 133.1, 132.8, 128.5, 127.5, 125.8, 123.2, 118.8 (d, *J*=7.9 Hz), 117.7 (d, *J*=8.4 Hz), 117.1 (d, *J*=23.6 Hz), 109.1 (d, *J*=24.4 Hz); MS (EI) *m*/*z* (%) 213 (100) [M$^+$], 185 (38), 184 (37), 164 (7), 157 (24); IR (KBr plate, cm^{-1}) ν 3436, 3035, 2878, 1686, 1664, 1507, 1369, 1269, 1151, 766.

*4.3.13. Thieno[3,2-c]quinolin-4(5H)-one (**2l**).*[37] 65% yield; ^{1}H NMR (500 MHz, CD_3SOCD_3, TMS) δ 11.75 (br s, 1H), 7.84 (d, *J*=8.0 Hz, 1H), 7.79 (d, *J*=5.0 Hz, 1H), 7.60 (d, *J*=5.5 Hz, 1H), 7.48–7.51 (m, 1H), 7.42–7.44 (m, 1H), 7.23–7.26 (m, 1H); ^{13}C NMR (125 MHz, CD_3SOCD_3, TMS) δ 158.1, 145.5, 136.2, 131.1, 129.3, 126.6, 125.2, 123.3, 122.4, 116.2, 116.1; MS (EI) *m*/*z* (%) 201 (100) [M$^+$], 173 (14), 155 (9), 127 (14); IR (KBr plate, cm^{-1}) ν 3436, 3152, 3017, 2883, 1664, 1655, 1591, 1325, 745.

*4.3.14. 9-Chlorophenanthridin-6(5H)-one (**2n′**).*[38] ^{1}H NMR (400 MHz, CD_3SOCD_3, TMS) δ 11.79 (br s, 1H), 8.61 (d, *J*=2.0 Hz, 1H), 8.45 (d, *J*=8.0 Hz, 1H), 8.31 (d, *J*=8.8 Hz, 1H), 7.68 (dd, *J*=8.6, 1.8 Hz, 1H), 7.53 (t, *J*=7.4 Hz, 1H), 7.37 (d, *J*=8.0 Hz, 1H), 7.27 (t, *J*=7.8 Hz, 1H); ^{13}C NMR (125 MHz, CD_3SOCD_3, TMS) δ 160.1, 138.2, 137.0, 136.1, 130.3, 129.7, 128.1, 124.4, 123.8, 122.4, 116.6, 116.2, 20.9; MS (EI) *m*/*z* (%) 229 (100) [M$^+$], 201 (9), 195 (23), 166 (41), 139 (32); IR (KBr plate, cm^{-1}) ν 3436, 3025, 2872, 1675, 1606, 1431, 1360, 834, 748.

*4.3.15. 10-Methylphenanthridin-6(5H)-one (**2p**).*[37] 57% yield; ^{1}H NMR (500 MHz, CD_3SOCD_3, TMS) δ 11.71 (br s, 1H), 8.45 (d, *J*=8.5 Hz, 1H), 8.33 (d, *J*=7.5 Hz, 1H), 7.72 (d, *J*=7.5 Hz, 1H), 7.54 (t, *J*=7.8 Hz, 1H), 7.50 (t, *J*=7.5 Hz, 1H), 7.42 (d, *J*=8.0 Hz, 1H), 7.27 (t, *J*=7.5 Hz, 1H), 2.93 (s, 3H); ^{13}C NMR (125 MHz, CD_3SOCD_3, TMS) δ 160.9, 137.0, 136.9, 135.1, 133.3, 128.7, 127.4, 127.3, 127.2, 126.0, 121.6, 118.8, 116.2, 25.6; MS (EI) *m*/*z* (%) 209 (100) [M$^+$], 190 (13), 180 (36), 165 (11), 152 (27); IR (KBr plate, cm^{-1}) ν 3436, 3110, 2970, 2894, 1654, 1597, 1512, 1372, 732, 692.

*4.3.16. 5-Phenylphenanthridin-6(5H)-one (**2r**).*[39] 52% yield; ^{1}H NMR (400 MHz, CD_3SOCD_3, TMS) δ 8.61 (d, *J*=8.0 Hz, 1H), 8.54 (dd, *J*=8.0, 1.2 Hz, 1H), 8.37 (dd, *J*=8.0, 1.2 Hz, 1H), 7.90–7.94 (m, 1H), 7.64–7.72 (m, 3H), 7.56–7.60 (m, 1H), 7.37–7.41 (m, 3H), 7.31–7.35 (m, 1H), 6.55 (dd, *J*=8.2, 1.0 Hz, 1H); ^{13}C NMR (100 MHz, CD_3SOCD_3, TMS) δ 160.4, 138.8, 138.2, 133.7, 133.2, 130.1, 129.5, 129.3, 128.7, 128.3, 128.0, 125.2, 123.6, 122.6, 122.6, 118.3, 116.4; MS (EI) *m*/*z* (%) 272 (16) [M+1]$^+$, 271 (86) [M$^+$], 270 (100) [M−1]$^+$, 241 (27), 151 (15), 140 (18), 139 (19), 77 (25), 50 (31), 43 (19), 39 (13); IR (KBr plate, cm^{-1}) ν 3058, 1656, 1605, 1584, 1486, 1345, 1321, 748, 723, 696.

4.4. General procedure for preparation of palladacycle A[19,24]

A suspension formed by 2-phenylaniline **1a** (507 mg, 3.0 mmol), $Pd(OAc)_2$ (672 mg, 3.0 mmol), and MeOH (20 mL) was stirred at room temperature for 24 h. The precipitate was filtered, washed with 10 mL of MeOH and 10 mL of diethyl ether, and dried under vacuum. A brown powder, 839 mg, yield: 84%. ^{1}H NMR (400 MHz, CD_3SOCD_3, TMS) δ 9.40 (br s, 2H), 7.59 (t, *J*=4.2 Hz, 1H), 7.49 (d, *J*=7.6 Hz, 1H), 7.43 (d, *J*=7.6 Hz, 1H), 7.20–7.22 (m, 2H), 7.08–7.17 (m, 3H), 1.81 (s, 3H); IR (KBr plate, cm^{-1}) ν 3436, 3234, 3048, 1578, 1560, 1495, 1418, 1022, 751, 739.

4.5. General procedure for synthesis of PJ34

*4.5.1. Preparation of 5-H-phenanthridin-6-one (**2a**).* The synthesis of **2a** is according to the method of carbonylation reaction. **2a** can be obtained in 81% isolated yield (790 mg) from **1a** (0.845 g, 5 mmol).

*4.5.2. 2-Nitrophenanthridin-6(5H)-one (**3a**).*[40] 5-*H*-Phenanthridin-6-one **2a** (975 mg, 5.0 mmol) was dissolved in 10 mL nitric acid with stirring for 12 h. A thick yellow precipitate formed. The mixture was filtered through a plug of Celite and the residue was washed with cold water (20 mL), ethyl ether (20 mL), dried under vacuum at 50 °C. The crude product **3a** was obtained in 83% yield (996 mg), which was used directly in the next step without further purification.

*4.5.3. 2-Aminophenanthridin-6(5H)-one (**4a**).*[28] The crude product **3a** was dissolved in DMF (20 mL), 10% NH_4Cl (15 mL) was added, followed by addition of iron powder (4.0 g). The mixture was stirring at 100 °C for 1 h. After cooled to room temperature, the mixture was filtered, and the filtrate was extracted three times with $CHCl_3$ (3×30 mL). The combined organic layers were washed with brine (40 mL), dried over anhydrous sodium sulfate, filtered, and concentrated. The residue was purified by flash column chromatography with ethyl acetate (EA) as eluent to afford 2-aminophenanthridin-6(5*H*)-one (**4a**)[13e] (410 mg, 65%). ^{1}H NMR (400 MHz, CD_3SOCD_3, TMS) δ 11.36 (br s, 1H), 8.30 (d, *J*=8.0 Hz, 1H), 8.21 (d, *J*=8.0 Hz, 1H), 7.81 (t, *J*=7.6 Hz, 1H), 7.59 (t, *J*=7.4 Hz, 1H), 7.47 (d, *J*=1.2 Hz, 1H), 7.10 (d, *J*=8.0 Hz, 1H), 6.82 (dd, *J*=8.4, 1.4 Hz, 1H), 5.03 (br s, 2H); ^{13}C NMR (125 MHz, CD_3SOCD_3, TMS) δ 160.5, 144.5, 134.7, 132.9, 128.2, 128.1, 127.9, 126.4, 122.6, 118.7, 118.3, 117.3, 106.4; MS (EI) *m*/*z* (%) 210 (100) [M$^+$], 181 (27), 154 (15), 127 (14); IR (KBr plate, cm^{-1}) ν 3450, 3359, 3001, 1652, 1606, 1512, 1470, 1420, 1378, 1156, 846, 776.

*4.5.4. 2-(Dimethylamino)-N-(6-oxo-5,6-dihydrophenanthridin-2-yl) acetamide (**PJ34**).*[41] To a 10 mL round flask was charged with **4a** (210 mg, 1.0 mmol), *N*,*N*′-dicyclohexylcarbodiimide (DCC, 412 mg, 2.0 mmol), *N*,*N*-dimethyl-pyridin-4-amine (DMAP, 6 mg, 5 mol %), *N*,*N*-Dimethylglycine (155 mg, 1.5 mmol), CH_2Cl_2 (2 mL). The mixture was stirring for 12 h at room temperature. Then the mixture was filtered through a plug of Celite and the residue was washed with ethyl acetate (3×20 mL). The filtrate was evaporated in vacuo. The residue was purified by flash column chromatography on silica gel with ethyl acetate (EA) and methanol (10:1) as eluent to afford the corresponding products **PJ34** (257 mg, 87%). ^{1}H NMR (400 MHz, CD_3SOCD_3, TMS) δ 11.69 (br s, 1H), 9.87 (br s, 1H), 8.69 (d, *J*=2.0 Hz, 1H), 8.31–8.35 (m, 2H), 7.87–7.91 (m, 1H), 7.83 (dd, *J*=8.8, 2.0 Hz, 1H), 7.66 (t, *J*=7.6 Hz, 1H), 7.32 (d, *J*=8.8 Hz, 1H), 3.13 (s, 2H), 2.33 (s, 6H); ^{13}C NMR (100 MHz, CD_3SOCD_3, TMS) δ 168.6, 160.5, 134.0, 133.6, 132.8, 132.6, 128.0, 127.6, 125.8, 122.2, 122.0, 117.4, 116.2, 113.4, 63.3, 45.4; MS (EI) *m*/*z* (%) 295 (3) [M$^+$], 209 (8), 182 (4), 153 (4), 127 (7), 58 (100), 42 (21); IR (KBr plate, cm^{-1}) ν 3431, 2929, 2852, 1654, 1576, 1461, 1384, 1150, 774.

Acknowledgements

Funding from National Basic Research Program of China (No. 2011CB936003) and NSFC (No. 21072169 and No. 21272205) is highly acknowledged. The work was also supported by the National Key Technology Research and Development Program (No. 2012BAK25B03).

Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tet.2013.05.025.

References and notes

1. For selected reviews, see:: (a) Colquhoun, H. M.; Thompson, D. J.; Twigg, M. V. *Carbonylation, Direct Synthesis of Carbonyl Compounds*; Plenum: New York, 1991; (b) Beller, M.; Cornils, B.; Frohning, C. D.; Kohlpaintner, C. W. *J. Mol. Catal. A: Chem.* **1995**, *104*, 17; (c) Beller, M. Carbonylation of Benzyl- and Aryl-X Compounds In *Applied Homogeneous Catalysis with Organometallic Compounds*, 2nd ed.; Cornils, B., Herrmann, W. A., Eds.; Wiley-VCH: Weinheim, 2002; (d) Brennführer, A.; Neumann, H.; Beller, M. *Angew. Chem., Int. Ed.* **2009**, *48*, 4114; (e) Wu, X.-F.; Neumann, H.; Beller, M. *Chem. Soc. Rev.* **2011**, *40*, 4986.
2. For selected examples of palladium-catalyzed carbonylations of organic halides, see:: (a) Schoenberg, A.; Heck, R. F. *J. Org. Chem.* **1974**, *39*, 3318; (b) Klaus, S.; Neumann, H.; Zapf, A.; Strübing, D.; Hübner, S.; Almena, J.; Riermeier, T.; Gross, P.; Sarich, M.; Krahnert, W.-R.; Rossen, K.; Beller, M. *Angew. Chem., Int. Ed.* **2006**, *45*, 154; (c) Martinelli, J. R.; Clark, T. P.; Watson, D. A.; Munday, R. H.; Buchwald, S. L. *Angew. Chem., Int. Ed.* **2007**, *46*, 8460; (d) McNulty, J.; Nair, J. J.; Robertson, A. *Org. Lett.* **2007**, *22*, 4575; (e) Neumann, H.; Brennführer, A.; Beller, M. *Chem.—Eur. J.* **2008**, *14*, 3645; (f) Zhang, Z.; Liu, Y.; Gong, M.; Zhao, X.; Zhang, Y.; Wang, J. *Angew. Chem., Int. Ed.* **2010**, *49*, 1139; (g) Wu, X.-F.; Neumann, H.; Spannenberg, A.; Schulz, T.; Jiao, H.; Beller, M. *J. Am. Chem. Soc.* **2010**, *132*, 14596.
3. For selected examples of palladium-catalyzed carbonylations of organic pseudohalides, see:: (a) Liu, Q.; Li, G.; He, J.; Liu, J.; Li, P.; Lei, A. *Angew. Chem., Int. Ed.* **2010**, *49*, 3371; (b) Wu, X.-F.; Neumann, H.; Beller, M. *Angew. Chem., Int. Ed.* **2010**, *49*, 5284.
4. (a) Fujiwara, Y.; Kawauchi, T.; Taniguchi, H. *J. Chem. Soc., Chem. Commun.* **1980**, 220; (b) Moore, E. J.; Pretzer, W. R.; O'Connell, T. J.; Harris, J.; LaBounty, L.; Chou, L.; Grimmer, S. S. *J. Am. Chem. Soc.* **1992**, *114*, 5888; (c) Brennführer, A.; Neumann, H.; Beller, M. *ChemCatChem* **2009**, *1*, 28; (d) Liu, Q.; Zhang, H.; Lei, A. *Angew. Chem., Int. Ed.* **2011**, *50*, 10788.
5. (a) Chatani, N.; Ie, Y.; Kakiuchi, F.; Murai, S. *J. Org. Chem.* **1997**, *62*, 2604; (b) Ie, Y.; Chatani, N.; Ogo, T.; Marshall, D. R.; Fukuyama, T.; Kakiuchi, F.; Murai, S. *J. Org. Chem.* **2000**, *65*, 1475; (c) Guan, Z.-H.; Ren, Z.-H.; Spinella, S. M.; Yu, S.; Liang, Y.-M.; Zhang, X. *J. Am. Chem. Soc.* **2009**, *131*, 729.
6. (a) Houlden, C. E.; Hutchby, M.; Bailey, C. D.; Ford, J. G.; Tyler, S. N. G.; Gagné, M. R.; Lloyd-Jones, G. C.; Booker-Milburn, K. I. *Angew. Chem., Int. Ed.* **2009**, *48*, 1830; (b) Giri, R.; Lam, J. K.; Yu, J.-Q. *J. Am. Chem. Soc.* **2010**, *132*, 686; (c) Yoo, E. J.; Wasa, M.; Yu, J.-Q. *J. Am. Chem. Soc.* **2010**, *132*, 17378.
7. (a) Inoue, S.; Shiota, H.; Fukumoto, Y.; Chatani, N. *J. Am. Chem. Soc.* **2009**, *131*, 6898; (b) Hasegawa, N.; Charra, V.; Inoue, S.; Fukumoto, Y.; Chatani, N. *J. Am. Chem. Soc.* **2011**, *133*, 8070.
8. (a) Orito, K.; Horibata, A.; Nakamura, T.; Ushito, H.; Nagasaki, H.; Yuguchi, M.; Yamashita, S.; Tokuda, M. *J. Am. Chem. Soc.* **2004**, *126*, 14342; (b) Vicente, J.; Saura-Llamas, I.; García-López, J.-A.; Calmuschi-Cula, B. *Organometallics* **2007**, *26*, 2768; (c) Vicente, J.; Saura-Llamas, I.; García-López, J.-A. *Organometallics* **2009**, *28*, 448; (d) Li, H.; Cai, G.-X.; Shi, Z.-J. *Dalton Trans.* **2010**, *39*, 10442; (e) Haffemayer, B.; Gulias, M.; Gaunt, M. J. *Chem. Sci.* **2011**, *2*, 312; (f) López, B.; Rodriguez, A.; Santos, D.; Albert, J.; Ariza, X.; Garcia, J.; Granell, J. *Chem. Commun.* **2011**, 1054.
9. Lu, Y.; Leow, D.; Wang, X.; Engle, K. M.; Yu, J.-Q. *Chem. Sci.* **2011**, *2*, 967.
10. Giri, R.; Yu, J.-Q. *J. Am. Chem. Soc.* **2008**, *130*, 14082.
11. (a) Asaumi, T.; Matsuo, T.; Fukuyama, T.; Ie, Y.; Kakiuchi, F.; Chatani, N. *J. Org. Chem.* **2004**, *69*, 4433; (b) Ma, B.; Wang, Y.; Peng, J.; Zhu, Q. *J. Org. Chem.* **2011**, *76*, 6362.
12. (a) D'Souza, D. M.; Müller, T. J. J. *Chem. Soc. Rev.* **2007**, *36*, 1095; (b) Church, T. L.; Byrne, C. M.; Lobkovsky, E. B.; Coates, G. W. *J. Am. Chem. Soc.* **2007**, *129*, 8156; (c) Tadd, A. C.; Fielding, M. R.; Willis, M. C. *Chem. Commun.* **2009**, 6744; (d) Cao, H.; Vieira, T. O.; Alper, H. *Org. Lett.* **2011**, *13*, 11; (e) Wu, X.-F.; Neumann, H.; Beller, M. *Chem.—Eur. J.* **2012**, *18*, 12599.
13. (a) Weltin, D.; Picard, V.; Aupeix, K.; Varin, M.; Oth, D.; Marchal, J.; Dufour, P.; Bischoff, P. *Int. J. Immunopharmacol.* **1995**, *17*, 265; (b) Holl, V.; Coelho, D.; Weltin, D.; Dufour, P.; Bischoff, P. *Anticancer Res.* **2000**, *20*, 3233; (c) Fujio, I.; Atsushi, A.; Mariko, I.; Masanori, M. JP 2002128762 A 20020509 *Jpn. Kokai Tokkyo Koho* **2002**, ; (d) Tu, Z.; Chu, W.; Zhang, J.; Dence, C. S.; Welch, M. J.; Mach, R. H. *Nucl. Med. Biol.* **2005**, *32*, 437; (e) Patil, S.; Kamath, S.; Sanchez, T.; Neamati, N.; Schinazi, R. F.; Buolamwini, J. K. *Bioorg. Med. Chem.* **2007**, *15*, 1212.
14. (a) Lehtiö, L.; Jemth, A.-S.; Collins, R.; Loseva, O.; Johansson, A.; Markova, N.; Hammarström, M.; Flores, A.; Holmberg-Schiavone, L.; Weigelt, J.; Helleday, T.; Schüler, H.; Karlberg, T. *J. Med. Chem.* **2009**, *52*, 3108; (b) Yam-Canul, P.; Chirino, Y. I.; Sánchez-González, D. J.; Martínez-Martínez, C. M.; Cruz, C.; Pedraza-Chaverri, J. *Basic Clin. Pharmacol. Toxicol.* **2008**, *102*, 483.
15. (a) Walls, L. P. *J. Chem. Soc.* **1935**, *10*, 1405; (b) Mosby, W. L. *J. Am. Chem. Soc.* **1954**, *76*, 936; (c) Pan, H.-L.; Fletcher, T. L. *J. Heterocycl. Chem.* **1970**, *2*, 313; (d) Elango, S.; Srinivasan, P. C. *Tetrahedron Lett.* **1993**, *34*, 1347.
16. Smith, P. A. S. *J. Am. Chem. Soc.* **1948**, *70*, 320.
17. Zhou, Q.; Worm, K.; Dolle, R. E. *J. Org. Chem.* **2004**, *69*, 5147.
18. Lu, S. M.; Alper, H. *J. Am. Chem. Soc.* **2005**, *127*, 14776.
19. Albert, J.; D'Andrea, L.; Granell, J.; Zafrilla, J.; Font-Bardia, M.; Solans, X. *J. Organomet. Chem.* **2007**, *692*, 4895.
20. (a) Liang, Z.; Ju, L.; Xie, Y.; Huang, L.; Zhang, Y. *Chem.—Eur. J.* **2012**, *18*, 15816; (b) Yu, M.; Xie, Y.; Xie, C.; Zhang, Y. *Org. Lett.* **2012**, *14*, 2164; (c) Yu, M.; Liang, Z.; Wang, Y.; Zhang, Y. *J. Org. Chem.* **2011**, *76*, 4987; (d) Cheng, K.; Yao, B.; Zhao, J.; Zhang, Y. *Org. Lett.* **2008**, *22*, 5309.
21. For more information about the optimization studies, see the Supplementary data.
22. Liang, D.; Hu, Z.; Peng, J.; Huang, J.; Zhu, Q. *Chem. Commun.* **2013**, 173.
23. More recently, a Pd(II)-catalyzed carbonylation protocol of *N*-sulfonyl-2-aminobiaryls for synthesis of *N*-tosyl phenanthri-dinones has been developed by Chuang etc. and the tosyl groups are preserved Rajeshkumar, V.; Lee, T.-H.; Chuang, S.-C. *Org. Lett.* **2013**, *15*, 1468.
24. Albert, J.; Granell, J.; Zafrilla, J.; Font-Bardia, M.; Solans, X. *J. Organomet. Chem.* **2005**, *690*, 422.
25. (a) Ryabov, A. D.; Sakodinskaya, I. K.; Yatsimirsky, A. K. *J. Chem. Soc., Dalton Trans.* **1985**, 2629; (b) Hennessy, E. J.; Buchwald, S. L. *J. Am. Chem. Soc.* **2003**, *125*, 12084; (c) Park, C.-H.; Ryabova, V.; Seregin, I. V.; Sromek, A. W.; Gevorgyan, V. *Org. Lett.* **2004**, *6*, 1159; (d) Lane, B. S.; Brown, M. A.; Sames, D. *J. Am. Chem. Soc.* **2005**, *127*, 8050; (e) Engle, K. M.; Wang, D.-H.; Yu, J.-Q. *J. Am. Chem. Soc.* **2010**, *132*, 14137.
26. (a) Zhu, B.; Angelici, R. J. *J. Am. Chem. Soc.* **2006**, *128*, 14460; (b) Díaz, D. J.; Darko, A. K.; McElwee-White, L. *Eur. J. Org. Chem.* **2007**, 4453.
27. Wurz, G.; Hofer, O.; Greger, H. *Nat. Prod. Lett.* **1993**, *3*, 177.
28. Szabo, C.; Japtap, P.; Southan, G.; Salzman, A. U.S. Patent 6,476,048, 2002.
29. Liu, L.; Zhang, Y.; Xin, B. *J. Org. Chem.* **2006**, *71*, 3994.
30. Youn, S. W.; Bihn, J. H. *Tetrahedron Lett.* **2009**, *50*, 4598.
31. Stokes, B. J.; Jovanović, B.; Dong, H.; Richert, K. J.; Riell, R. D.; Driver, T. G. *J. Org. Chem.* **2009**, *74*, 3225.
32. Taylor, E. C.; Strojny, E. J. *J. Am. Chem. Soc.* **1956**, *78*, 5104.
33. Bernini, R.; Cacchi, S.; Fabrizi, G.; Sferrazzaa, A. *Synthesis* **2008**, *5*, 729.
34. Pan, H.-L.; Fletcher, T. L. *J. Heterocycl. Chem.* **1970**, *7*, 313.
35. Woodroofe, C. C.; Zhong, B.; Lu, X.; Silverman, R. B. *J. Chem. Soc., Perkin Trans. 2* **2000**, 55.
36. Fujta, R.; Yoshisuji, T.; Wakayanagi, S.; Wakamatsu, H.; Matsuzaki, H. *Chem. Pharm. Bull.* **2006**, *54*, 204.
37. Bhakuni, B. S.; Kumar, A.; Balkrishna, S. J.; Sheikh, J. A.; Konar, S.; Kumar, S. *Org. Lett.* **2012**, *14*, 2838.
38. Al-Jalal, N. A.; Ibrahim, M. R.; Al-Awadi, N. A.; Elnagdi, M. H. *Molecules* **2011**, *16*, 10256.
39. Furuta, T.; Kitamura, Y.; Hashimoto, A.; Fujii, S.; Tanaka, K.; Kan, T. *Org. Lett.* **2007**, *9*, 183.
40. Meseroll, L. M. N.; McKee, J. R.; Zanger, M. *Synth. Commun.* **2011**, *41*, 2557.
41. Magan, N.; Isaacs, R. J.; Stowell, K. M. *Anti-Cancer Drugs* **2012**, *23*, 627.