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Graphical Abstract

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Synthesis of Phenanthridinones Using Cu- or Pd-mediated C-N Bond Formation

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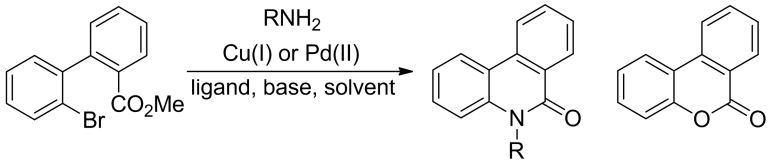

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ABSTRACT

The chemoselective synthesis of phenanthridinones was studied using copper(I)- and palladium(II)-catalyzed C-N bond formation with various bases, ligands, and solvents. Phenanthridinones were obtained from 2-halobiarylcarboxylates and amines in a one-pot reaction. The phenanthridinones and heterocyclic-fused lactam derivatives were accomplished using developed methods.

1. Introduction

Phenanthridinone scaffold has been found widely in various biologically active compounds.[1-4] In 1893, phenanthridinone was first synthesized by Grabe and Wander using Hofmann reaction of 2,2'-amidobiphenylcarboxylic acid but the unsatisfied yield was obtained.[5] The Curtius degradation of diphenic monoazide in alcoholic solvent under the acid condition was then developed, leading to the phenanthridinone derivative but there remained limitations of variation of its analog.[6-7] The syntheses of phenanthridinones have been further studied for more effective routes.[8-12] Since the C-N bond formations have been conducted by Buchwald and Hartwig groups, palladium-catalyzed C-N bond formations using the necessary ligand and base were reported for more efficient conditions to construct the nitrogen containing compounds.[13-18]

Phenanthridinone is a common moiety found in bioactive alkaloids from many sources as shown in Fig. 1. Oxynitidine (**1**), a phenanthridinone derived from *Xanthoxylum*, is a potential antitumor and antiviral agent.[19] Pancratistatin (**2**), shows a high level of inhibition of *in vivo* cancer cell growth.[20] Indenoisoquinoline (**3**) acts as a non-camptothecin topoisomerase I inhibitor.[21] Azalamellarin D (**4**) is an extension of lamellarin D (**5**) investigated in our group.[22] The lactam within the B-ring of an azalamellarin replaces the lactone structure of lamellarin, improving the compound's stability.[22] Lamellarin D (**5**) has received attention from many research groups, including ours.[23] Biological and synthetic studies of lamellarin D in particular have been reported.[24]

Reported herein is a methodology for the one-pot synthesis of a small-molecule lactam model that is analogous to the core of many pharmacologically active compounds. Developing an efficient synthesis for this lactam will aid in optimizing reaction conditions for biologically active phenanthridinone derivatives, with a heterocyclic-fused lactam.

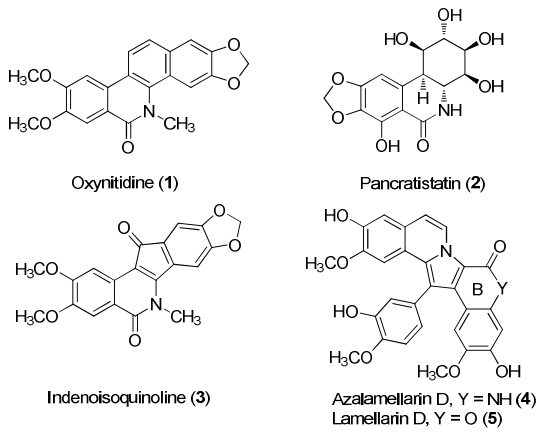


Figure 1. Structures of oxynitidine (**1**), pancratistatin (**2**), indenoisoquinoline (**3**), azalamellarin D (**4**), and lamellarin D (**5**).

2. Results and discussion

2.1. Cu(I)-mediated lactone and lactam formation: Completion of C-O and C-N bond formation

Methyl 2-bromocarboxylate (**6**) and homoveratylamine (**7**) were used to study the Cu(I)-catalyzed C-N bond formation of the corresponding phenanthridinone **8**.[22,25] Various bases and bidentate ligands (**a** to **e** in Fig. 2) were screened with the subcritical water under the benign conditions to conform with the green chemistry aspect.[26] The competition of intermolecular C-N bond formation and intramolecular C-O bond formation was observed and afforded a mixture of the target compound **8** and benzopyranone **9** in moderate to good yields as summarized in the Table 1.

First, we examined the possibility of Cu(I)-catalyzed C-N bond formation of compounds **6** and **7** with subcritical water at 300 °C using copper thiophenecarboxylate (CuTC) as catalyst in the presence of Cs_2CO_3 as a base.[26] The C-N bond formation product, lactam **8** and C-O bond formation product, lactone **9** were obtained in 23% and 36% yields, respectively (Table 1, entry 1). The bidentate ligands **a-e** were screened and it was found that TMEDA (ligand **a**) gave the C-N bond formation product **8** in higher yield (Table 1, entry 2) compared with other bidentate ligands **b-e** which gave lactone **9** in higher yield (Table 1, entries 3 to 6). Some bases were then screened in the presence of TMEDA (ligand **a**), and gave lower yield of the corresponding lactam **8** (Table 1, entries 7 and 8). Interestingly, using phosphazine base *t*-Bu-P_4 as base in the absence of ligand, the highest overall yield was obtained in a 1:2 ratio of lactam **8**: lactone **9** (Table 1, entry 9). Adjusting the amounts of amine **7** (3 to 10 equivalents) under basic conditions and TMEDA as ligand, both lactam **8** and lactone **9** yields relatively increased (Table 1, entries 10 to 12). It was summarized that the intramolecular C-O bond formation occurred faster than the intermolecular C-N bond formation using subcritical water; this is in good accordance with our previous report.[26]

In an attempt to synthesize phenanthridione as the major product, the chemoselectivity of C-N bond formation was studied based on the result of entry 2 Table 1 that gave compound 8 as a major product using 0.5 equiv CuTC, in the presence of Cs_2CO_3 and TMEDA. We then optimized the conditions by screening other solvents with the different dielectric constant for microwave irradiation. To our delight, the ratio of compounds **8:9** increased to 1.7:1 ratio using dioxane as solvent (Table 2, entry 1). When the solvent was changed to DMF, the yield of mixture **8** and **9** increased, in a 1:1 ratio (Table 2, entry 2). A mixture of water and DMF or toluene in a 1:1 ratio resulted in the decrease in the ratio of C-N bond formation product (Table 2, entries 3 to 4). Interestingly, reaction carried out in toluene gave C-O bond formation in excellent yield (Table 2, entry 5) whereas using dichloromethane, methanol or solvent free condition gave no reaction (Table 2, entries 6 to 8). Among different size of alkyl groups, methyl ester gave the best result (Table 2, entries 9 and 10).

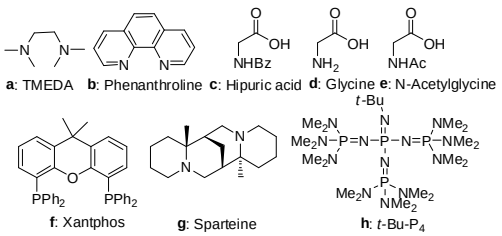
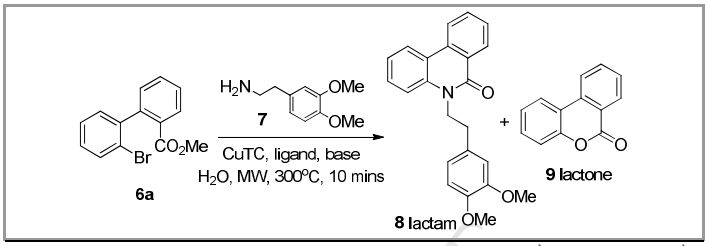


Figure 2. Screened ligands **a-g** and phophazine base **h** in this study.

Table 1. Reaction of methyl-2-bromocarboxylate **6a** and homoveratylamine **7** mediated by CuTC in the subcritical water condition, use various bases and ligands.[a]

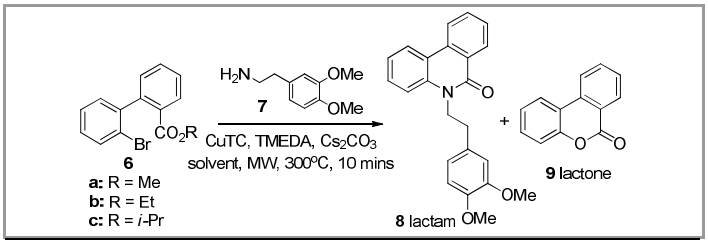


Entry	**7** (equiv)	Base	Ligand	Yield **8** (%)[b]	Yield **9** (%)[b]
1	5	Cs_2CO_3	-	23	36
2	5	Cs_2CO_3	a	31	18
3	5	Cs_2CO_3	b	9	41
4	5	Cs_2CO_3	c	23	50
5	5	Cs_2CO_3	d	10	37
6	5	Cs_2CO_3	e	11	38
7	5	K_2CO_3	a	26	33
8	5	NaO*t*-Bu	a	16	34
9	5	*t*-Bu-P_4	-	31	60
10	3	Cs_2CO_3	a	20	36
11	7	Cs_2CO_3	a	34	36
12	10	Cs_2CO_3	a	34	49

[a] Unless otherwise noted, the reactions were performed in a 10 mL microwave vessel: 0.5 equiv of CuTC, 300 °C, 10 min. The 300 °C reactions should only be performed by a trained chemist using a dedicated, scientific reactor with adequate safety features.

[b] Isolated yields of pure product after PTLC on silica.

Table 2. Screening of solvents and alkyl groups.[a]



Entry	compound	Solvent	Yield **8** (%)[b]	Yield **9** (%)[b]
1	**6a**	Dioxane	17	10
2	**6a**	DMF	25	24
3	**6a**	H_2O:DMF 1:1	25	51
4	**6a**	H_2O:Toluene 1:1	18	31
5	**6a**	Toluene	trace	95
6	**6a**	DCM	NR[c]	NR[c]
7	**6a**	MeOH	NR[c]	NR[c]
8	**6a**	-[d]	NR[c]	NR[c]
9	**6b**	H_2O	23	39
10	**6c**	H_2O	19	18

[a] Unless otherwise noted, the reactions were performed in a 10 mL microwave vessel: 5 equiv of homoveratrylamine, 0.5 equiv of CuTC, 300 °C, 10 min. The 300 °C reactions should only be performed by a trained chemist using a dedicated, scientific reactor with adequate safety features.

[b] Isolated yields of pure product after PTLC on silica.

[c] NR: no reaction.

[d] Solvent-free reaction.

2.2. Pd(II)-mediated C-N bond formation

The competition of Cu(I)-mediated C-N and C-O bond formation gave a mixture of phenanthridinone **8** and benzopyranone **9** under microwave irradiation. To study the selectivity of C-N bond formation, we then turned our interest to the palladium catalyst. The reaction of methyl 2-bromocarboxylate (**6a**) and homoveratylamine (**7**) was studied using Pd(II)-catalyzed C-N bond formation with various bases and ligands as shown in Table 3.

We initially attempted to use 5 mol% $Pd(OAc)_2$, 10 mol% Xantphos (ligand **f**) and Cs_2CO_3 in 1,4-dioxane under microwave irradiation at 300 ^oC for 10 min and obtained only the C-O bond formation of benzopyranone **9** in 60% yield (Table 3, entry 1). A dramatic change took place when using conventional heating at 115 ^oC for 23 h; thus, the double C-N bond formation product **8** was obtained in moderate yield (55% yield) together with the undesired product, carbazole **10** in 35% yield (Table 3, entry 2). Increasing the amount of catalyst gave no significant increase in the yield of product **8** and carbazole **10** (Table 3, entry 3) as well as using $Pd(TFA)_2$ as a catalyst, instead of $Pd(OAc)_2$ (Table 3, entry 4). The yield of **8** increased to 76% yield using 5 mol% $PdCl_2$, 10 mol% Xantphos and Cs_2CO_3 in refluxing 1,4-dioxane at 115 ^oC (Table 3, entry 5). A detailed screening of different bases revealed that using Cs_2CO_3 gave the highest yield of phenanthridinone 8. Sparteine (ligand **g**) was also studied instead of Xantphos (ligand **f**) and gave lower yield (Table 3, entry 10).

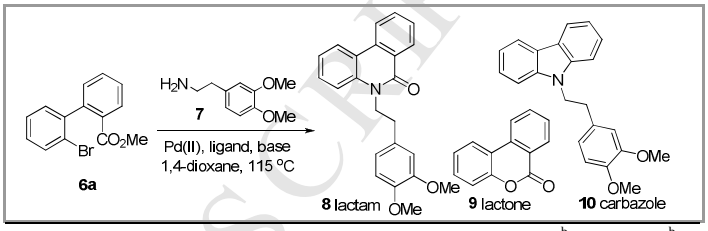
The tentative mechanism of C-N bond formation of compounds **8** and **10** is proposed as shown in Scheme 1. The oxidative addition of a palladium complex inserted into the C-Br bond of **6a** and followed by reacting with amine to form the intermediate **B**. The reductive elimination of **B** afforded the C-N bond formation product **C** which was further lactamized to give the target product **8**.[27] The carbazole **10** was obtained by the tandem decarboxylative palladium-catalyzed intramolecular C-N bond formation.[28-29] It may arise from palladium complex **E** produced by the palladium-catalyzed decarboxylation and initial oxidative addition of carboxylate **D** followed by either the second oxidative addition to form palladacycle[30] **F** or palladium complex **G** which underwent reductive elimination to give carbazole **10**.

With the effective conditions for the synthesis of phenanthridinone **8** in hand, we then directed our attention to the synthesis of a small library of phenanthridinone analogues using both 5 mol% $PdCl_2$ (condition A) and 10 mol% $Pd(TFA)_2$ (condition B) as the catalyst, Xantphos as ligand, and Cs_2CO_3 as base in refluxing 1,4-dioxane at 115 ^oC. The phenanthridinone analogues **11-17** were obtained in 12-86% yields as shown in Table 4. The *N*-benzylated phenanthridinone **11** was obtained in 45% and 86% yields using $PdCl_2$ and $Pd(OAc)_2$ as catalyst, respectively (Table 4, entries 1 to 2). The electron donating group such as methoxy group in the benzylamine derivative affected to the yield of Pd-catalyzed C-N bond formation products (Table 4, entries 3 to 6).

2.3. Pd(II)-mediated C-N bond formation: Synthesis of phenanthridinone derivatives

In order to demonstrate our strategy in the synthesis of a heterocyclic-fused lactam, we synthesized a small group of phenanthridinone derivatives using the optimized condition as shown in Table 5. The polyoxygenated phenanthridinones **24** and **25** were prepared from methyl tri- and tetra-methoxybiarylcarboxylates **18** and **19**, respectively, in poor to moderate yields (Table 5, entries 1-4). The results of conditions A, with $PdCl_2$ as catalyst, gave the products **24** and **25** in higher yield than condition B. Heteroaromatic-fused lactam, tetracyclic 7-methyl-*5H*-indolo[2,3-*c*]quinolin-6(*7H*)-one **26** and 11-methyl-*5H*-indolo[3,2-*c*]quinolin-6(*11H*)-one **27** were successfully obtained from the corresponding 2-arylindole-3-carboxylate **20** and 3-arylindole-2-carboxylate **21** in poor to moderate yields using conditions A (Table 5, entries 5-6). Benzo[*h*][1,6]-naphthyridin-5(6*H*)-one **28** was prepared from 2-arylnicotinate **22** in moderate yield (Table 5, entries 7-8). Synthesis of the last heterocyclic compound, furo[2,3-*c*]quinolin-4(5H)-one **29** was achieved from 2-arylfuran-3-carboxylate **23** in poor yield under both conditions (Table 5, entries 9 and 10).

Table 3. Screening of palladium(II), bases and ligands.

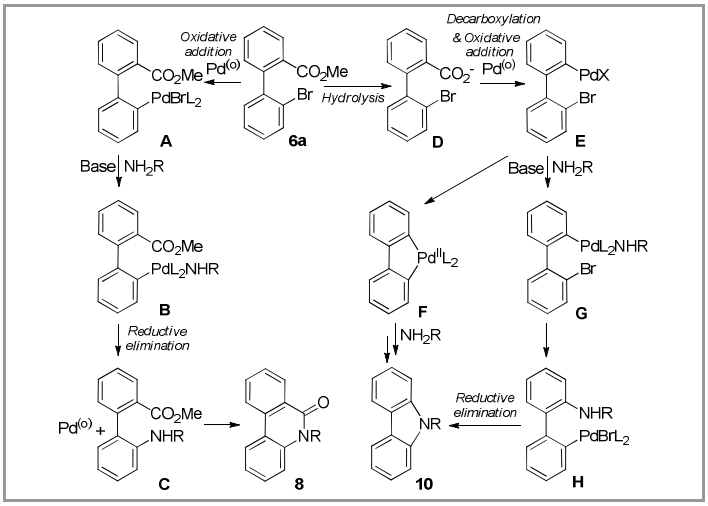


Entry	Pd(II) (mol%)	Base	Ligand (mol%)	Time (h)	**8**[b] (%)	**9(10)**[b] (%)
1[a]	$Pd(OAc)_2$ (5)	Cs_2CO_3	f (10)	0.16	-	**9**, 60
2	$Pd(OAc)_2$ (5)	Cs_2CO_3	f (10)	23	55	**10**, 35
3	$Pd(OAc)_2$ (10)	Cs_2CO_3	f (20)	23	53	**10**, 32
4	$Pd(TFA)_2$ (10)	Cs_2CO_3	f (20)	23	45	**10**, 31
5	$PdCl_2$ (5)	Cs_2CO_3	f (10)	23	76	trace
6	$PdCl_2$ (5)	Na_2CO_3	f (10)	23	NR[c]	-
7	$PdCl_2$ (5)	K_2CO_3	f (10)	23	25	-
8	$PdCl_2$ (5)	Ag_2CO_3	f (10)	23	NR[c]	-
9	$PdCl_2$ (5)	K_3PO_4	f (10)	23	NR[c]	-
10	$PdCl_2$ (5)	Cs_2CO_3	g (10)	23	45	-

[a] The reactions were performed in a 10 mL microwave vessel, 300 ^oC, 10 min. The 300 ^oC reactions should only be performed by a trained chemist using a dedicated, scientific reactor with adequate safety features.

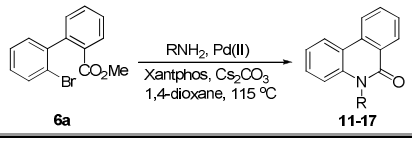
[b] Isolated yields of pure product after PTLC on silica.

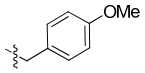
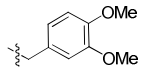
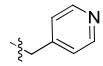
[c] NR: no reaction.



Scheme 1. A proposed mechanism.

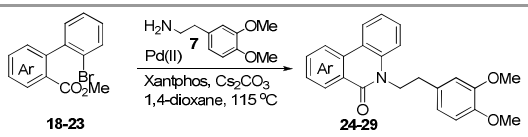
Table 4. Synthesis of phenanthridin-4-one derivatives.

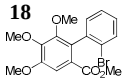
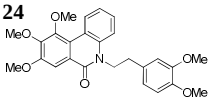
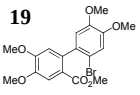
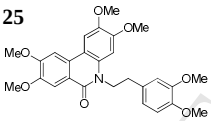
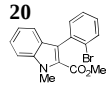
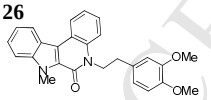
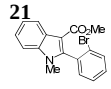
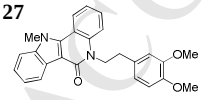
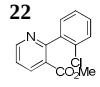
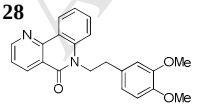
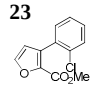
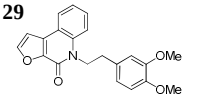


Entry	R	Pd(II) (mol%)	Time (h)	Product (%)[a]
1		$PdCl_2$ (5)	23	**11**, 45
2		$Pd(OAc)_2$ (10)	23	**11**, 86
3		$PdCl_2$ (5)	57	**12**, 34
4		$Pd(OAc)_2$ (10)	23	**12**, 75
5		$PdCl_2$ (5)	23	**13**, 12
6		$Pd(OAc)_2$ (10)	23	**13**, 29
7		$PdCl_2$ (5)	23	**14**, 11
8		$Pd(OAc)_2$ (10)	28	**14**, 26
9		$PdCl_2$ (5)	23	**15**, 65
10		$Pd(OAc)_2$ (10)	29	**15**, 6
11		$PdCl_2$ (5)	69	**16**, 32
12		$Pd(OAc)_2$ (10)	55	**16**, 2
13		$PdCl_2$ (5)	23	**17**, 32
14		$Pd(OAc)_2$ (20)	23	**17**, 64

[a] Isolated yields of pure product after PTLC on silica.

Table 5. Synthesis of various lactam derivatives.



Entry	Substrate	Product	cond[a]	Time (h)	Yield (%)[b]
1	**18** 	**24** 	A	12	48
2			B	30	8[c]
3	**19** 	**25** 	A	17	40
4			B	60	26
5	**20** 	**26** 	A	17	55
6	**21** 	**27** 	A	17	13
7	**22** 	**28** 	A	17	26
8			B	17	53
9	**23** 	**29** 	A	85	4
10			B	40	9

[a] All reactions were performed with palladium(II) catalyst (0.1 equiv), $PdCl_2$ for condition A and $Pd(OAc)_2$ for condition B, with biaryl ester (1.0 equiv), amine (5.0 equiv), Cs_2CO_3 (2.0 equiv), Xantphos (0.2 equiv) in 1,4-dioxane (5 mL).

[b] Isolated product yields after PTLC on silica gel.

[c] Recovered starting material 81%.

3. Conclusion

In summary, we have developed a new method using a Pd(II)-catalyzed coupling/lactamization process to construct phenanthridinones from various 2-halobiarylcarboxylates. The efficiency and functional group effects were studied and applied to a number of phenanthridinones and heterocyclic-fused quinolinone derivatives. This approach is a particularly efficient route to heterocyclic and polycyclic quinolinone scaffolds.

4. Experimental section

4.1. General methods

Melting points were measured with a Thermo Fisher Scientific IA920 digital melting point apparatus and reported without correction. ^{1}H-Nuclear magnetic resonance (^{1}H NMR) spectra were recorded on a Varian Gemini2000, a Bruker AV-300, and a Bruker Avance-600 NMR instruments at 200, 300, and 600 MHz, respectively, using deuterochloroform as solvents with tetramethylsilane as an internal standard. ^{13}C-Nuclear magnetic resonance (^{13}C NMR) spectra were recorded on a Varian Gemini2000, a Bruker AV-300, and a Bruker Avance-600 NMR instruments at 50, 75, and 150 MHz, respectively, using deuterochloroform with tetramethylsilane as an internal standard. FTIR spectra were obtained on a Spectrum One FTIR spectrometer, a Perkin Elmer System with the universal ATR (UATR) accessory. Mass spectra were performed with an AEI-MS-902. High-resolution mass spectra were performed with a MicroTOF$_{LC}$, Bruker Daltonics. Column chromatography was carried out using Fluka aluminum oxide (type 507 C neutral; 100-125 mesh) and Merck silica gel (70-230 mesh ASTM). Thin layer chromatography (TLC) and preparative thin layer chromatography (PTLC) were carried out on precoated silica gel (E. Merck PF 254). All reagents were purified and dried according to the standard procedures.

4.2. General Procedure for the Preparation of Biarylcarboxylate Esters 6a - 6c and 18 - 23

A solution of 2-halophenylboronic acid (2.0 equiv), alkyl 2-bromophenylcarboxylate (1.0 equiv) and 10 mol% $Pd(PPh_3)_4$ in three portion of toluene:EtOH:10%Na_2CO_3 (5:1:2) solution was refluxed overnight. After the complete reaction was observed by TLC, water was added to quench and partition with EtOAc to obtain the crude product. The crude product was then purified by flash column chromatography or the preparative thin layer chromatography (10% EtOAc:hexanes) to obtain the product. Spectroscopic data of the biarylcarboxylate esters including compounds **6a**, **18 – 21**,[24] **22** and **23**[25] were previously reported in the literature.

*4.2.1. Ethyl 2'-bromo-[1,1'-biphenyl]-2-carboxylate (**6b**).* Employing the general procedure with ethyl 2-bromobenzoate (0.10 g, 0.32 mmol) with 2-bromophenylboronic acid (0.13 g, 0.65 mmol) under the general condition above gave **6b** as pale colorless oil (0.07 g, 78% yield). R_f 0.45 (20% EtOAc:hexanes). IR (UATR): ν_{max} 3053, 2981, 1714, 1600, 1465, 1443, 1365, 1287, 1255, 1131, 752 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.95 (dd, J = 7.5, 1.2 Hz, 1H), 7.52 (dd, J = 8.1, 1.2 Hz, 1H), 7.48 (dt, J = 7.5, 1.5 Hz, 1H), 7.38 (dt, J = 8.7, 1.5 Hz, 1H), 7.25 (dt, J = 7.0, 1.2 Hz, 1H), 7.17 – 7.09 (m, 3H), 4.00 (q, J = 6.0 Hz, 2H), 0.92 (t, J = 6.0 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 167.0, 142.9, 142.0, 132.0, 131.6, 130.8, 130.4, 130.2, 130.0, 128.5, 127.8, 126.9, 123.0, 60.8, 13.6. HRMS (microTOF): m/z calcd for $C_{15}H_{13}{}^{81}BrO_2Na$ (M[^{81}Br]+Na$^+$): 328.9972, found 328.9972; for $C_{15}H_{13}{}^{79}BrO_2Na$ (M[^{79}Br]+Na$^+$): 326.9983; found 326.9991.

*4.2.2. Isopropyl 2'-bromo-[1,1'-biphenyl]-2-carboxylate (**6c**).* Employing the General Procedure with isopropyl 2-bromobenzoate (0.10 g, 0.41 mmol) with 2-bromophenylboronic acid (0.16 g, 0.82 mmol) under the general condition above gave **6c** as a colorless oil

(0.02 g, 22% yield). R_f 0.42 (20% EtOAc:hexanes). IR (UATR): ν_{max} 3058, 2979, 2934, 1708, 1600, 1464, 1414, 1350, 1285, 1257, 1106, 750 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 8.02 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.59 (d, *J* = 8.1 Hz, 1H), 7.54 (dt, *J* = 7.5, 1.5 Hz, 1H), 7.45 (dt, *J* = 7.6, 1.2 Hz, 1H), 7.32 (dt, *J* = 6.9, 1.2 Hz, 1H), 7.24 – 7.17 (m, 3H), 4.97 (sept, *J* = 6.3 Hz, 1H), 1.04 (d, *J* = 6.3 Hz, 3H), 0.95 (d, *J* = 6.3 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.7, 143.2, 141.9, 132.1, 131.5, 131.0, 130.8, 130.2 (2C), 128.6, 127.9, 126.9, 123.2, 68.3, 21.4, 21.3. HRMS (microTOF): m/z calcd for $C_{16}H_{15}{}^{81}BrO_2Na$ (M[^{81}Br]+Na^+): 343.0132, found 343.0128; for $C_{16}H_{15}{}^{79}BrO_2Na$ (M[^{79}Br]+Na^+): 341.0143; found 341.0147.

4.3. General Procedure for the Preparation of Phenanthridinones 8, 11 – 17 and 24 – 29

A mixture of methyl 2-halobiarylcarboxylate (0.2 mmol, 1.0 equiv), amine (1.0 mmol, 5.0 equiv), $PdCl_2$ (0.02 mmol, 0.1 equiv), xantphos (0.02 mmol, 0.1 eqiuv), and Cs_2CO_3 (0.4 mmol, 2.0 eqiuv) in 1,4-dioxane (5 mL) was heated at 115 °C under Ar atmosphere for 12 to 85 h. The reaction was monitored by TLC. After completion, the reaction was partitioned with water (25 mL) and EtOAc (4 x 25 mL). The solvent was removed under reduced pressure to give a crude product which was then purified by PTLC (30% EtOAc/hexane) to give the product.

4.3.1. 5-(3,4-Dimethoxybenzyl)phenanthridin-6(5H)-one ***(8)****.* Employing the general procedure with compound **6a** (0.10 g, 0.34 mmol), homoveratrylamine (**7**) (0.20 mL, 1.71 mmol), Xantphos (0.02 g, 0.03 mmol), $PdCl_2$ (0.005 g, 0.02 mmol) and Cs_2CO_3 (0.22 g, 0.68 mmol) in 1,4-dioxane (5 mL) for 23 h gave a yellow solid (0.09 g, 76 % yield). R_f 0.28 (30% EtOAc:hexanes). Mp: 94 – 97 °C. IR (UATR): ν_{max} 2935, 2827, 1645, 1608, 1587, 1514, 1438, 1259, 1237, 1155, 1027 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 8.52 (d, *J* = 7.8 Hz, 1H), 8.20 (d, *J* = 7.8 Hz, 1H), 8.19 (d, *J* = 8.1 Hz, 1H), 7.69 (t, *J* = 7.2 Hz, 1H), 7.54 (t, *J* = 7.8 Hz, 1H), 7.50 (t, *J* = 8.1 Hz, 1H), 7.40 (d, *J* = 8.1 Hz, 1H), 7.26 (t, *J* = 7.2 Hz, 1H), 6.91 – 6.80 (m, 3H), 4.52 (t, *J* = 7.8 Hz, 2H), 3.85 (s, 6H), 2.99 (t, *J* = 7.8 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 161.0, 148.9, 147.6, 136.7, 133.3, 132.2, 130.9, 129.4, 128.4, 127.7, 125.2, 123.3, 122.1, 121.3, 120.5, 119.2, 114.6, 111.9, 111.3, 55.7 (2C), 44.2, 33.0. EI-MS: *m/z* (%) 359 (M^+, 3), 178 (31), 164 (100), 151 (11), 149 (24). HRMS (microTOF): *m/z* calcd for $C_{23}H_{21}NO_3Na$ (M + Na^+) 382.1411; found 382.1413.

4.3.2. 5-(Benzyl)phenanthridin-6(5H)-one ***(11)****.* Employing the general procedure with compound **6a** (0.06 g, 0.20 mmol), benzylamine (0.10 mL, 1.03 mmol), Xantphos (0.01 g, 0.02 mmol), $PdCl_2$ (0.003 g, 0.01 mmol) and Cs_2CO_3 (0.13 g, 0.41 mmol) in 1,4-dioxane (5 mL) for 23 h gave a yellow solid (0.02 g, 45% yield). R_f 0.34 (20% EtOAc:hexanes). Mp: 115 – 117 °C. IR (UATR): ν_{max} 3027, 1650, 1608, 747, 723 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 8.53 (d, *J* = 7.8 Hz, 1H), 8.20 (m, 2H), 7.69 (t, *J* = 7.8 Hz, 1H), 7.52 (t, *J* = 7.8 Hz, 1H), 7.32 – 7.18 (m, 8H), 5.57 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 161.9, 137.3, 136.6, 133.8, 132.7, 129.5, 129.1, 128.8 (2C), 128.0, 127.1, 126.5 (2C), 125.4, 123.3, 122.5, 121.7, 119.5, 116.0, 46.5. EI-MS: *m/z* (%) 286 ($M+H^+$, 7), 285 (34), 284 (19), 179 (22), 167 (27), 97 (29), 83 (24). HRMS (microTOF): *m/z* calcd for $C_{20}H_{15}NONa$ (M + Na^+) 308.1055; found 308.1045.

4.3.3. 5-(4-Methoxybenzyl)phenanthridin-6(5H)-one ***(12)****.* Employing the general procedure with compound **6a** (0.06 g, 0.20 mmol), 4-methoxybenzylamine (0.13 mL, 1.03 mmol), Xantphos (0.01 g, 0.02 mmol), $PdCl_2$ (0.003 g, 0.0.01 mmol) and Cs_2CO_3 (0.13 g, 0.41 mmol) in 1,4-dioxane (5 mL) for 57 h gave a yellow solid (0.02 g, 34% yield). R_f 0.20 (10% EtOAc:hexanes). Mp: 129 – 131 °C. IR (UATR): ν_{max} 2956, 2925, 2852, 1646, 1608, 1512, 1437, 1246, 1031, 724 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 8.61 (d, *J* = 8.1 Hz, 1H), 8.29 – 8.10 (m, 2H), 7.77 (t, *J* = 7.5 Hz, 1H), 7.60 (t, *J* = 7.8 Hz, 1H), 7.42 – 7.19 (m, 5H), 6.81 (d, *J* = 8.1 Hz, 2H), 5.59 (s, 2H), 3.73 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 161.9, 158.7, 137.3, 133.8, 132.6, 129.5, 129.1, 128.6, 128.0, 127.9 (2C), 125.5, 123.2, 122.5, 121.6, 119.5, 116.0, 114.2 (2C), 55.2, 45.9. EI-MS: *m/z* (%) 316 (M^+, 7), 315 (32), 166 (7), 149 (8), 121 (100). HRMS (microTOF): *m/z* calcd for $C_{21}H_{17}NO_2Na$ (M + Na^+) 338.1150; found 338.1151.

4.3.4. 5-(3,4-Dimethoxybenzyl)phenanthridin-6(5H)-one ***(13)****.* Employing the general procedure with compound **6a** (0.06 g, 0.20 mmol), 3,4-dimethoxybenzylamine (0.15 mL, 1.03 mmol), Xantphos (0.01 g, 0.02 mmol), $PdCl_2$ (0.003 g, 0.01 mmol) and Cs_2CO_3 (0.13 g, 0.41 mmol) in 1,4-dioxane (5 mL) for 23 h gave a yellow solid (0.008 g, 12% yield). R_f 0.25 (20% EtOAc:hexanes). Mp: 118 – 120 °C. IR (UATR): ν_{max} 2934, 1722, 1646, 1608, 1514, 1437, 1258, 1139, 1025 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 8.62 (d, *J* = 7.8 Hz, 1H), 8.32 – 8.25 (m, 2H), 7.79 (t, *J* = 7.5 Hz, 1H), 7.62 (t, *J* = 7.5 Hz, 1H), 7.44 – 7.28 (m, 3H), 6.86 (s, 1H), 6.77 (m, 2H), 5.60 (s, 2H), 3.81 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 161.9, 154.5, 149.4, 148.2, 137.4, 133.8, 132.7, 129.5, 129.1, 128.0, 125.4, 123.3, 122.6, 121.7, 119.5, 118.8, 116.0, 111.4, 110.1, 55.9 (2C), 46.3. EI-MS: *m/z* (%) 345 (M^+, 33), 167 (24), 151 (100), 127 (11), 97 (19), 71 (28). HRMS (microTOF): *m/z* calcd for $C_{22}H_{19}NO_3Na$ (M + Na^+) 368.1249; found 368.1257.

4.3.5. 5-(Pyridin-2-ylmethyl)phenanthridin-6(5H)-one ***(14)****.* Employing the general procedure with compound **6a** (0.06 g, 0.20 mmol), pyridine-2-ylmethanamine (0.10 mL, 1.03 mmol), Xantphos (0.01 g, 0.02 mmol), $PdCl_2$ (0.003 g, 0.01 mmol) and Cs_2CO_3 (0.13 g, 0.41 mmol) in 1,4-dioxane (5 mL) for 23 h gave a white solid (0.013 g, 11 % yield). R_f 0.25 (20% EtOAc:hexanes). Mp: 137 – 139 °C. IR (UATR): ν_{max} 3066, 1650, 1608, 1587, 1436, 1316 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 8.63 – 8.61 (m, 2H), 8.29 (m, 2H), 7.79 (td, *J* = 7.6, 1.5 Hz, 1H), 7.62 (t, *J* = 7.8 Hz, 1H), 7.54 (td, *J* = 7.6, 1.5 Hz, 1H), 7.47 – 7.37 (m, 2H), 7.27 (td, *J* = 7.8, 1.5 Hz, 1H), 7.17 – 7.14 (m, 2H), 5.78 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 161.8, 156.9, 149.3, 137.3, 137.0, 133.9, 132.7, 129.6, 129.1, 128.0, 125.3, 123.2, 122.7, 122.3, 121.7, 121.4, 119.4, 116.2, 48.6. EI-MS: *m/z* (%) 286 (M^+, 100), 269 (73), 180 (81), 149 (66). HRMS (microTOF): *m/z* calcd for $C_{19}H_{15}N_2O$ (M + H^+) 287.1176; found 287.1178.

4.3.6. 5-(Pyridin-3-ylmethyl)phenanthridin-6(5H)-one ***(15)****.* Employing the general procedure with compound **6a** (0.08 g, 0.29 mmol), pyridine-3-ylmethanamine (0.10 mL, 1.47 mmol), Xantphos (0.01 g, 0.02 mmol), $PdCl_2$ (0.004 g, 0.01 mmol) and Cs_2CO_3 (0.19 g, 0.59 mmol) in 1,4-dioxane (5 mL) for 23 h gave a yellow solid (0.05 g, 65% yield). R_f 0.17 (20% EtOAc:hexanes). Mp: 104 – 106 °C. IR (UATR): ν_{max} 2920, 2851, 1649, 1608, 1436, 1366, 1335, 1313, 749, 742 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 8.66 (s, 1H), 8.60 (d, *J* = 8.1 Hz, 1H), 8.49 (br s, 1H), 8.30 (d, *J* = 7.8 Hz,, 2H), 7.80 (t, *J* = 7.8 Hz, 1H), 7.63 (t, *J* = 7.5 Hz, 1H), 7.54 (d, *J* = 7.8 Hz, 1H), 7.42 (t, *J* = 7.5 Hz, 1H), 7.32 – 7.18 (m, 3H), 5.68 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.9, 148.8, 148.5, 137.1, 134.5, 133.8, 132.9, 132.4, 129.7, 129.1, 128.2, 125.2, 123.6, 123.5, 122.8, 121.8, 119.6, 115.5, 44.1. EI-MS: *m/z* (%) 286 (M^+, 92), 285 (100), 269 (49), 179 (36), 166 (17), 149 (11), 92 (41). HRMS (microTOF): *m/z* calcd for $C_{19}H_{15}N_2O$ (M + H^+) 287.1174; found 287.1178.

4.3.7. 5-(Pyridin-4-ylmethyl)phenanthridin-6(5H)-one ***(16)****.* Employing the general procedure with compound **6a** (0.06 g, 0.20 mmol), pyridine-4-ylmethanamine (0.10 mL, 1.03 mmol), Xantphos (0.01 g, 0.02 mmol), $PdCl_2$ (0.003 g, 0.01 mmol) and Cs_2CO_3 (0.13 g, 0.41 mmol) in 1,4-dioxane (5 mL) for 69 h gave a white solid (0.018 g, 32% yield). R_f 0.22 (20% EtOAc:hexanes). Mp: 96 – 99 °C. IR (UATR): ν_{max} 3524, 3034, 2946, 1646, 1608, 1584, 1587, 1435, 1362, 749 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 8.67 (br s, 1H), 8.59 (dd, *J* = 7.9, 1.2 Hz, 1H), 8.51 (br s, 1H), 8.28 (d, *J* = 8.1 Hz, 2H), 7.79 (td, *J* = 7.6, 1.5 Hz, 1H), 7.61 (t, *J* = 7.2 Hz, 1H), 7.54 (d, *J* = 7.8 Hz, 1H), 7.41 (td, *J* = 7.8, 1.2 Hz, 1H), 7.30 – 7.18 (m, 3H), 5.66 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 161.8, 148.6, 148.4, 136.8,

134.6, 133.7, 132.9, 129.7, 129.0, 128.1, 125.1, 123.8, 123.5, 122.8 (2C), 121.7, 119.5, 115.4, 44.0. EI-MS: *m/z* (%) 286 (M^+, 12), 279 (12), 167 (27), 149 (98), 97 (40), 69 (100). HRMS (microTOF): *m/z* calcd for $C_{19}H_{14}N_2ONa$ (M + Na^+) 309.0993; found 309.0998.

*4.3.8. 5-(3-Methylpyridin-2-yl)phenanthridin-6(5H)-one (**17**).* Employing the general procedure with compound **6a** (0.08 g, 0.29 mmol), 3-methylpyridin-2-ylamine (0.11 mL, 1.47 mmol), Xantphos (0.01 g, 0.02 mmol), $PdCl_2$ (0.004 g, 0.01 mmol) and Cs_2CO_3 (0.19 g, 0.59 mmol) in 1,4-dioxane (5 mL) for 23 h gave a yellow solid (0.025 g, 32% yield). R_f 0.11 (20% EtOAc:hexanes). Mp: 178 – 180 °C. IR (UATR): ν_{max} 3059, 2920, 2815, 1654, 1607, 1435, 1319, 748, 724 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ 8.83 – 8.75 (m, 2H), 8.58 – 8.50 (m, 2H), 8.06 – 8.00 (m, 2H), 7.82 (t, *J* = 8.0 Hz, 1H), 7.63 (dd, *J* = 7.7, 4.6 Hz, 1H), 7.53 – 7.47 (m, 2H), 6.65 – 6.60 (m, 1H), 2.36 (s, 3H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 160.9, 150.7, 148.1, 140.2, 137.4, 134.2, 132.9, 132.7, 129.3, 128.8, 128.0, 125.7, 124.5, 123.2, 122.9, 121.8, 119.1, 115.6, 17.0. EI-MS: *m/z* (%) 286 (M^+, 46), 285 (100), 271 (12), 255 (9). HRMS (microTOF): *m/z* calcd for $C_{19}H_{15}N_2O$ (M + H^+) 287.1174; found 287.1178.

*4.3.9. 5-(3,4-Dimethoxyphenethyl)-8,9,10-trimethoxyphenan thridin-6(5H)-one (**24**).* Employing the general procedure with compound **18** (0.02 g, 0.06 mmol), homoveratrylamine (**7**) (0.11 mL, 0.65 mmol), Xantphos (0.007 g, 0.01 mmol), $PdCl_2$ (0.002 g, 0.006 mmol) and Cs_2CO_3 (0.15 g, 0.45 mmol) in 1,4-dioxane (5 mL) for 12 h gave a yellow solid (0.01 g, 48% yield). R_f 0.48 (20% EtOAc:hexanes). Mp: 102 – 104 °C. IR (UATR): ν_{max} 3498, 2928, 2850, 1714, 1642, 1606, 1582, 1515, 1454, 1143, 1085, 754 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 9.23 (d, *J* = 8.4 Hz, 1H), 7.96 (s, 1H), 7.60 – 7.45 (m, 2H), 7.35 (t, *J* = 7.5 Hz, 1H), 6.96 – 6.85 (m, 3H), 4.58 (t, *J* = 8.2 Hz, 2H), 4.04 (s, 3H), 4.03 (s, 3H), 3.97 (s, 3H), 3.89 (s, 2 x 3H), 3.04 (t, *J* = 8.2 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 160.7, 153.3, 151.4, 149.1, 147.8, 147.3, 136.0, 131.1, 128.4, 127.3, 122.7, 122.4, 121.6, 120.7, 119.2, 114.4, 112.0, 111.4, 106.1, 61.2, 60.4, 56.1, 55.9 (2C), 44.9, 33.2. EI-MS: *m/z* (%) 449 (M^+, 5), 298 (8), 286 (17), 185 (100), 164 (50), 149 (50). HRMS (microTOF): *m/z* calcd for $C_{26}H_{27}NO_6Na$ (M + Na^+) 472.1735; found 472.1730.

*4.3.10. 5-(3,4-Dimethoxyphenethyl)-2,3,8,9-tetramethoxy phenanthridin-6(5H)-one (**25**).* Employing the general procedure with compound **19** (0.02 g, 0.06 mmol), homoveratrylamine (**7**) (0.10 mL, 0.60 mmol), Xantphos (0.007 g, 0.01 mmol), $PdCl_2$ (0.002 g, 0.006 mmol) and Cs_2CO_3 (0.13 g, 0.42 mmol) in 1,4-dioxane (5 mL) for 17 h gave a yellow solid (0.01 g, 40% yield). R_f 0.08 (20% EtOAc:hexanes). Mp: 180 – 182 °C. IR (UATR): ν_{max} 2997, 2936, 2830, 1633, 1611, 1588, 1509, 1257, 1028 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.95 (s, 1H), 7.54 (s, 1H), 7.42 (s, 1H), 6.82 – 6.88 (m, 4H), 4.59 (t, *J* = 8.1 Hz, 2H), 4.11 (s, 3H), 4.05 (s, 6H), 3.98 (s, 3H), 3.87 (s, 3H), 3.84 (s, 3H), 3.06 (t, *J* = 8.1 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 160.7, 153.3, 150.3, 149.2 (2C), 147.9, 145.0, 131.5, 131.3, 128.3, 120.5, 118.5, 112.1 (2C), 111.5, 108.9, 105.4, 102.0, 98.7, 56.6, 56.1 (2C), 55.9 (2C), 55.8, 44.9, 33.5. EI-MS: *m/z* (%) 479 (M^+, 0), 279 (12), 167 (26), 149 (100), 97 (10). HRMS (microTOF): *m/z* calcd for $C_{27}H_{29}NO_7Na$ (M + Na^+) 502.1841; found 502.1836.

*4.3.11. 5-(3,4-Dimethoxyphenethyl)-7-methyl-5H-indolo[2,3-c]quinolin-6(7H)-one (**26**).* Employing the general procedure with compound **20** (0.05 g, 0.14 mmol), homoveratrylamine (**7**) (0.10 mL, 0.72 mmol), Xantphos (0.008 g, 0.01 mmol), $PdCl_2$ (0.002 g, 0.007 mmol) and Cs_2CO_3 (0.09 g, 0.29 mmol) in 1,4-dioxane (5 mL) for 17 h gave a yellow solid (0.032 g, 55% yield). R_f 0.34 (30% EtOAc:hexanes). Mp: 136 – 140 °C. IR (UATR): ν_{max} 3053, 2929, 2850, 1643, 1514, 1463, 1260, 1155, 1028, 744 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 8.48 (d, *J* = 7.8 Hz, 1H), 8.39 (d, *J* = 7.8 Hz, 1H), 7.59 – 7.49 (m, 4H), 7.45 – 7.30 (m, 2H), 7.45 – 6.86 (m, 3H), 4.61 (t, *J* = 7.9 Hz, 2H), 4.38 (s, 3H), 3.90 (s, 6H), 3.05 (t, *J* = 7.9 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.6, 149.1, 147.8, 140.7, 135.1, 131.1, 126.2, 126.1, 125.9, 124.0, 122.6, 122.4, 121.6, 121.0, 120.7, 119.9, 118.6, 114.7, 112.1, 111.5, 110.5, 55.9 (2C), 43.9, 33.6, 31.5. EI-MS: *m/z* (%) 412 (M^+, 7), 248 (42), 129 (28), 97 (66), 69 (100). HRMS (microTOF): *m/z* calcd for $C_{26}H_{24}N_2O_3Na$ (M + Na^+) 435.1673; found 435.1679.

*4.3.12. 5-(3,4-Dimethoxyphenethyl)-11-methyl-5H-indolo[3,2-c]quinolin-6(11H)-one (**27**).* Employing the general procedure with compound **21** (0.02 g, 0.05 mmol), homoveratrylamine (**7**) (0.05 mL, 0.24 mmol), Xantphos (0.006 g, 0.01 mmol), $PdCl_2$ (0.002 g, 0.006 mmol) and Cs_2CO_3 (0.13 g, 0.40 mmol) in 1,4-dioxane (5 mL) for 17 h gave a brown solid (0.003 g, 13% yield). R_f 0.14 (30% EtOAc : hexane). R_f 0.14 (30% EtOAc:hexanes). Mp: 69 – 71 °C. IR (UATR): ν_{max} 3746, 3053, 2917, 2849, 1643, 1512, 1463, 743 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): 8.62 (d, *J* = 7.7 Hz, 1H), 8.45 (d, *J* = 8.1 Hz, 1H), 7.63 – 7.61 (m, 2H), 7.54 - 7.53 (m, 1H), 7.50 (t, *J* = 7.9 Hz, 1H), 7.41 (t, *J* = 8.9 Hz, 1H), 7.39 – 7.34 (m, 1H), 6.97 – 6.91 (m, 2H), 6.87 (d, *J* = 7.9 Hz, 1H), 4.67 (t, *J* = 8.4 Hz, 2H), 4.32 (s, 3H), 3.91 (s, 3H), 3.89 (s, 3H), 3.07 (t, *J* = 8.4 Hz, 2H). ^{13}C NMR (150 MHz, $CDCl_3$): 159.7, 149.3, 148.0, 140.0, 139.4, 138.6, 131.4, 130.1, 128.9, 124.6, 124.4, 123.2, 122.3, 122.0, 121.3, 120.8, 115.6, 114.9, 112.5, 111.7, 108.9, 56.0 (2C), 43.7, 33.7 (2C). EI-MS: *m/z* (%) 413 (M+H^+, 0), 88 (11), 86 (65), 84 (100), 83 (10). HRMS (microTOF): *m/z* calcd for $C_{26}H_{24}N_2O_3Na$ (M + Na^+) 435.1673; found 435.1679.

*4.3.13. 6-(3,4-Dimethoxyphenethyl)benzo[h][1,6]naphthyridin-5(6H)-one (**28**).* Employing the general procedure with compound **22** (0.10 g, 0.40 mmol), homoveratrylamine (**7**) (0.30 mL, 2.0 mmol), Xantphos (0.05 g, 0.08 mmol), $PdCl_2$ (0.007 g, 0.08 mmol) and Cs_2CO_3 (0.92 g, 2.82 mmol) in 1,4-dioxane (5 mL) for 17 h gave a white solid (0.04 g, 26% yield). R_f 0.20 (30% EtOAc:hexanes). R_f 0.20 (30% EtOAc : Hexane). Mp: 146 – 148 °C. IR (UATR): ν_{max} 2992, 2932, 2830, 1650, 1609, 1595, 1515, 756 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): 9.02 (dd, *J* = 4.5, 1.7 Hz, 1H), 8.95 (dd, *J* = 7.9, 1.4 Hz, 1H), 8.77 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.66 (td, *J* = 7.7, 1.5 Hz, 1H), 7.53 (dd, *J* = 7.9, 4.5 Hz, 1H), 7.48 (d, *J* = 8.4 Hz, 1H), 7.40 (t, *J* = 7.5 Hz, 1H), 6.92 – 6.84 (m, 3H), 4.59 (t, *J* = 8.3 Hz, 2H), 3.88 (s, 3H), 3.04 (t, *J* = 8.3 Hz, 2H). ^{13}C NMR (150 MHz, $CDCl_3$): 161.3, 153.8, 150.3, 149.3, 148.1, 138.3, 136.6, 131.3, 131.0, 125.7, 123.0, 122.8, 120.9 (2C), 120.8, 114.4, 112.4, 111.7, 56.0 (2C), 44.3, 33.2. EI-MS: *m/z* (%) 361 (M+H^+, 0), 360 (M^+, 2), 179 (19), 165 (13), 164 (98), 149 (39), 88 (10), 84 (100). HRMS (microTOF): *m/z* calcd for $C_{22}H_{21}NO_3$ (M + H^+) 361.1546; found 361.1546.

*4.3.14. 5-(3,4-Dimethoxyphenethyl)furo[2,3-c]quinolin-4(5H)-one (**29**).* Employing the general procedure with compound **23** (0.02 g, 0.10 mmol), homoveratrylamine (**7**) (0.08 mL, 0.52 mmol), Xantphos (0.006 g, 0.01 mmol), $PdCl_2$ (0.005 g, 0.01 mmol) and Cs_2CO_3 (0.07 g, 0.21 mmol) in 1,4-dioxane (5 mL) for 85 h gave a brown (1 mg, 4% yield). R_f 0.11 (30% EtOAc:hexanes). Mp: 77 – 79 °C. IR (UATR): ν_{max} 2918, 2849, 1646, 1515, 1145, 757 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): 8.06 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.64 (d, *J* = 1.9 Hz, 1H), 7.57 (dt, *J* = 7.8, 1.6 Hz, 1H), 7.50 (d, *J* = 8.5 Hz, 1H), 7.33 (t, *J* = 7.2 Hz, 1H), 7.09 (d, *J* = 1.9 Hz, 1H), 6.91 – 6.82 (m, 3H), 4.57 (t, *J* = 8.1 Hz, 2H), 3.87 (s, 2 x 3H), 2.99 (t, *J* = 8.8 Hz, 2H). ^{13}C NMR (150 MHz, $CDCl_3$): 159.2, 155.3, 144.0, 131.1, 129.5, 126.2, 122.2, 121.5, 120.8, 115.4, 114.9, 113.5, 112.4, 111.7, 108.3, 56.0 (2C), 43.9, 33.7, two quaternary carbons were not observed on the spectrum. EI-MS: *m/z* (%) 350 (M+H^+, 0), 164 (11), 149 (27), 88 (10), 86 (65), 84 (100). HRMS (microTOF): *m/z* calcd for $C_{21}H_{20}NO_4$ (M + Na^+) 350.1383; found 350.1386.

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