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Palladium-Catalyzed Intramolecular C−H Activation/C−C Bond Formation: A Straightforward Synthesis of Phenanthridines

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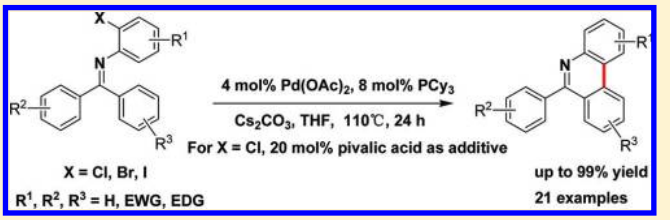
Supporting Information

ABSTRACT: The palladium-catalyzed intramolecular C−H activation/C−C cross-coupling has been developed for a straightforward and efficient synthesis of phenanthridines. With $Pd(OAc)_2$ (4 mol %) as the catalyst, PCy_3 (8 mol %) as the ligand, and Cs_2CO_3 as the base, this protocol was applied to synthesize a small library of phenanthridine derivatives in good yields in THF.



Phenanthridines are frequently found in a diverse array of compounds, including a wide range of significant natural products, biologically and therapeutically active compounds such as antiviral, antiprotozoal, and antitumor agents, and functional materials.[1] Molecules containing this motif have received considerable attention in medicinal and material chemistry; therefore, much effort has been focused on the synthetic methods of phenanthridine derivatives. Radical,[2] one-pot cascade,[3] benzyne-mediated,[4] photochemical,[5] hypervalent iodine-promoted,[6] photocyclized,[7] microwave-assisted,[2c,8] and transition-metal-catalyzed[9] syntheses of the phenanthridine skeleton have been reported.[10]

Palladium-catalyzed carbon−carbon bond-forming reactions involving direct C−H bond activation have emerged as powerful tools for the assembly of complex polycyclic structures.[11] The Fagnou group developed an operationally simple catalyst system for direct intramolecular arylation processes to form six- and five-membered ring biaryls.[12] More recently, Lautens reported a palladium-catalyzed cascade involving norbornene-mediated C−H activation/cross-coupling for the construction of diversely substituted phenanthridine derivatives.[13] Fensterbank et al. developed a dual palladium-catalyzed process for the efficient synthesis of phenanthridines from benzylamines and aryl iodides by coupling a palladium/norbornene co-catalyzed domino sequence with an oxidative dehydrogenation.[14]

Although a number of useful synthetic protocols are available for the preparation of phenanthridines, there remain many limitations such as multistep synthetic reactions, limited substrate scope, and, in some cases, harsh reaction conditions. Therefore, the development of more milder, general, and convenient processes using readily accessible building blocks for the synthesis of the phenanthridine ring system is imperative. In parallel with our efforts to develop more versatile and simpler synthetic methods of heterocycles,[15] herein we report on palladium-catalyzed intramolecular C−H activation/C−C cross-coupling reaction of *N*-(2-haloaryl)-imines for the direct and efficient synthesis of phenanthridines.

N-(2-bromophenyl)imine (**1a**) derived from the addition of 2-bromobenzenamine to benzophenone was selected as a model substrate for a palladium-catalyzed intramolecular C−H activation/C−C cross-coupling reaction. The blank experiment (without the catalyst and ligand) of **1a** was examined in toluene at 110 °C for 24 h using Cs_2CO_3 as the base, and no desired product was obtained (entry 1, Table 1). After an initial screen of various palladium catalysts (4 mol %) with PPh_3 (8 mol %) as the ligand, we found that the use of $Pd(OAc)_2$ gave the best result in 36% yield (entries 2−5, Table 1). To optimize other reaction conditions, different ligands, solvents, bases, reaction time, and temperature were examined using 4 mol % $Pd(OAc)_2$ as the catalyst, as shown in Table 1. It was known that palladium-catalyzed C−H activation/C−C bond-forming reactions using aryl halides as substrates are very sensitive to catalyst structure and ligand.[12b] Therefore, a judicious choice of ligands is needed to increase the yield of **2a**. We then investigated the effect of various ligands ($P(o\text{-tolyl})_3$, PCy_3, NHCs, bidentate phosphorus ligands such as dppm, dppb, dppf and xantphos) on the reaction (entries 6−12, Table 1). $Pd(OAc)_2$ and PCy_3 were found to be the combination for this cross-coupling reaction with the best yield (entry 8, Table 1). A survey of reaction media showed that the use of THF as solvent provided better results than those obtained in toluene, DMSO, and 1,2-dichloroethane (entries 8 and 13−15, Table 1). Reactions carried out in DMF gave a comparable yield to the reaction in THF (96 vs 98%, entries 13 and 16, Table 1). Finally, other bases such as K_2CO_3, pyridine, K_3PO_4, and

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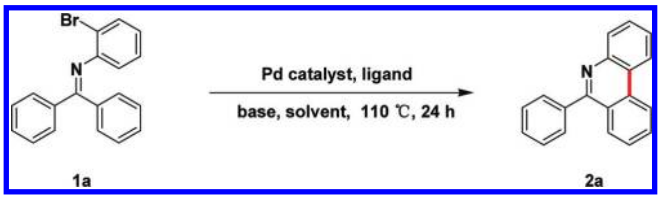
Table 1. Optimization of Palladium-Catalyzed Intramolecular C−C Cross-Coupling of Imine 1a[a]



entry	catalyst[b]	ligand[b]	base	solvent[b]	yield[c]
1			Cs_2CO_3	toluene	
2	$Pd_2(dba)_3$	PPh_3	Cs_2CO_3	toluene	trace
3	$PdCl_2$	PPh_3	Cs_2CO_3	toluene	trace
4	$PdCl_2(CH_3CN)_2$	PPh_3	Cs_2CO_3	toluene	19
5	$Pd(OAc)_2$	PPh_3	Cs_2CO_3	toluene	36
6	$Pd(OAc)_2$	P(*o*-tolyl)$_3$	Cs_2CO_3	toluene	39
7	$Pd(OAc)_2$	Ipr·HCl	Cs_2CO_3	toluene	19
8	$Pd(OAc)_2$	PCy_3	Cs_2CO_3	toluene	48
9	$Pd(OAc)_2$	xantphos	Cs_2CO_3	toluene	4
10	$Pd(OAc)_2$	dppm	Cs_2CO_3	toluene	40
11	$Pd(OAc)_2$	dppb	Cs_2CO_3	toluene	26
12	$Pd(OAc)_2$	dppf	Cs_2CO_3	toluene	44
13	$Pd(OAc)_2$	PCy_3	Cs_2CO_3	THF	98/92[d]/70[e]/66[f]
14	$Pd(OAc)_2$	PCy_3	Cs_2CO_3	DMSO	trace
15	$Pd(OAc)_2$	PCy_3	Cs_2CO_3	DCE	trace
16	$Pd(OAc)_2$	PCy_3	K_2CO_3	DMF	96
17	$Pd(OAc)_2$	PCy_3	K_2CO_3	THF	95
18	$Pd(OAc)_2$	PCy_3	Pyridine	THF	61
19	$Pd(OAc)_2$	PCy_3	KO^{t}Bu	THF	56
20	$Pd(OAc)_2$	PCy_3	K_3PO_4	THF	20

[a]Reaction conditions: 1.0 equiv of *N*-(2-bromophenyl)imine **1a** (1.0 mmol), 2.0 equiv of base, 4 mol % of Pd catalyst, 8 mol % of ligand, solvent (2 mL). [b]Abbreviations: dba = dibenzylideneacetone, IPr·HCl = 1,3-(2,6-diisopropylphenyl) imidazolium chloride, dppm = 1,1-bis-(diphenylphosphino)methane, xantphos = 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene, dppb = 1,4-bis(diphenylphosphino) butane, dppf = 1,1′-bis(diphenylphosphino)ferrocene, DMF = dimethylformamide, DCE = 1,2-dichloroethane. [c]Yield of isolated product after chromatography. [d]2 mol % of catalyst and 4 mol % of ligand were used. [e]1 mol % of catalyst and 2 mol % of ligand were used. [f]Performed at 80 °C.

KO^{t}Bu were examined, Cs_2CO_3 and K_2CO_3 provided better results (entries 17−20, Table 1).

Encouraged by the optimization results, we then explored the scope and generality of the present process. The nature of the ortho-substituted halogen on the *N*-aryl moiety was very important to the reaction outcome, shown in Table 2. Both the bromide and iodide analogues smoothly underwent the cyclization to afford the desired product in high to excellent yields; however, the use of aryl chloride to effect such transformations afforded inferior results (20% yield) under similar reaction conditions (entry 2, Table 2). The superior reactivity of the chloride analogues can be obtained to provide the product in 95.5% yield with the combined use of an insoluble Cs_2CO_3 and a catalytic quantity of soluble carboxylate base (in this case via deprotonation of the 20 mol % pivalic acid in situ).[16] Substitutions on the *N*-aryl moiety, such as Me, Cl, or CN were applicable, affording the cyclized products in good yields (entries 4−6, Table 2).

Imine substrates **1** with diverse substitutions on the benzophenone moiety were examined in this process. Some results from that study are summarized in Table 3. This method is efficient for the synthesis of a number of phenanthridines **2** in moderate to excellent yields. Aryl chlorides usually afforded inferior results than their bromo analogues, even with Cs_2CO_3 or K_2CO_3/*t*BuCO$_2$H as the base (entries 2 and 3, 8 and 9, Table 3). The syntheses of hindered phenanthridines were also facilitated by this catalyst system as demonstrated by entries 1, 8, 9, and 14 in Table 3. For aryl bromides, the electronic nature of the aromatic motifs involved in the C−H activation process did not seem to affect the efficiency of this transformation (entries 1, 2, 4, and 5, Table 3). It is worth noting that C−Cl compatible with reactions are particularly appealing because this substituent offers great opportunities for further cross-coupling reactions (entries 5 and 13, Table 3; entry 5, Table 2). *meta*-Methyl-substituted imine substrate **1o** participated in the C−C cross-coupling reaction effectively, giving an 83% yield of a mixture of two regioisomers (2:1, entry 14, Table 3). An analogous substrate (*Z*)-**1m** exhibited the same trend with sterically hindered aryl-substituted regioisomer as the main product (**2m′**:**2m″** = 1.5:1, entry 12, Table 3). Heteroaryl-substituted imine substrate (*Z*)-**1p** reacted at the 2-position of thiophene to afford the phenanthridine-like product in high yield (entry 15, Table 3).

A proposed reaction mechanism of palladium-catalyzed intramolecular C−C bond formation of *N*-aryl imines to phenanthridines was shown in Scheme 1. Initial oxidative addition of the aryl bromide or iodide to Pd(0) followed by approach of the aromatic ring led to a concerted metalation-deprotonation (CMD) transition state.[12,17] Subsequent reductive elimination produced the phenanthridine product and regenerated the active catalytic species. For aryl chloride, oxidative addition was followed by a chloride/pivalate ligand exchange, the latter enabling a CMD transition state to form the palladacycle. Palladacycle intermediate underwent C−C bond-forming reductive elimination to afford the desired product.

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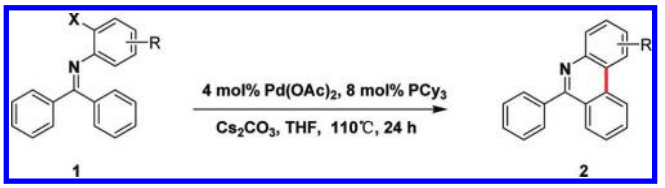
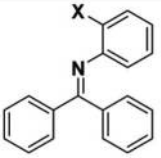
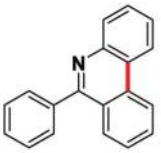
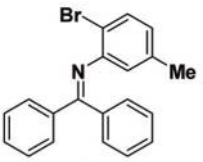
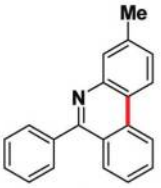
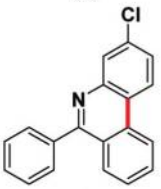
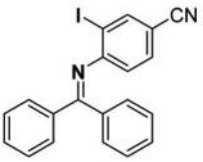
Table 2. Intramolecular Cyclization of Aryl Halides[a]



entry	substrate	product	yield (%)[b]
1	 1a X = Br	 2a	98
2	1a' X = Cl		20 (95.5)[c]
3	1a'' X = I		99
4	 1b	 2b	72
5	 1c	 2c	89
6	 1d	 2d	91

[a]Reaction conditions: *N*-(2-halophenyl)imine **1** (1.0 equiv, 1.0 mmol), Cs_2CO_3 (2.0 equiv), 4 mol % of $Pd(OAc)_2$, 8 mol % of PCy_3, THF (2 mL), 110 °C, 24 h. [b]Yield of isolated product after chromatography. [c]20 mol % 2,2-dimethylpropionic acid was added.

In summary, we described an efficient and simple protocol for the synthesis of phenanthridine derivatives via palladium-catalyzed intramolecular C−H activation/carbon−carbon bond formation. The results presented here, together with previous palladium-catalyzed processes, should be of considerable interest for the valuable synthetic building blocks for medicinal and material science.

EXPERIMENTAL SECTION

General Procedures for Palladium-Catalyzed Intramolecular C−C Bond-Forming Reaction of *N*-(*o*-Halophenyl)imines. A 10 mL Schlenk tube equipped with a magnetic stirring bar was charged with *N*-(*o*-halophenyl)-imine substrates[18] (1.0 mmol, 1.0 equiv), $Pd(OAc)_2$ (0.04 mmol, 9.0 mg), PCy_3 (0.08 mmol, 22.4 mg), PivOH (0.2 mmol, 20.4 mg, if added), and Cs_2CO_3 (652 mg, 2.0 mmol, 2.0 equiv), and then 2.0 mL of THF was added via syringe at room temperature. The tube was purged with nitrogen, sealed, and put into a preheated oil bath at 110 °C for 24 h. The reaction mixture was cooled to room temperature, quenched with water (3 mL), and diluted with ethyl acetate (5 mL). The layers were separated, and the aqueous layer was extracted with (2 × 5 mL) ethyl acetate. The combined organic extracts were dried over anhydrous sodium sulfate, filtered, and concentrated in vacuo. The crude residue was then purified by flash chromatography on silica gel (H) to afford the corresponding product, eluting with 10% ethyl acetate/petroleum ether.

6-Phenylphenanthridine (2a).[3c] Pale yellow solid: mp 103.5−104.5 °C; IR (KBr) ν (cm^{-1}) 3056, 3017, 2923, 2851, 1609, 1579, 1560, 1522, 1482, 1457, 1443, 1359, 1328, 1300, 1229, 1135, 1071, 956, 782, 755, 764, 726, 700, 671; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.72 (m, 1H), 8.65 (d, 1H, J = 8.0 Hz), 8.28−8.30 (m, 1H), 8.13 (d, 1H, J = 8.0 Hz), 7.90−7.86 (m, 1H), 7.81−7.70 (m, 4H), 7.66−7.54 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 161.3, 143.8, 139.8, 133.4, 130.5, 130.4, 129.7, 128.9, 128.8, 128.7, 128.4, 127.1, 126.9, 125.2, 123.7, 122.2, 121.9. HRMS-ESI (m/z): [M + Na]$^+$ calcd for $C_{19}H_{13}NNa$ 278.0946; found 278.0949.

3-Methyl-6-phenylphenanthridine (2b).[19] Yellow solid: mp 107−108 °C; IR (KBr) ν (cm^{-1}) 3055, 2922, 2854, 1609,

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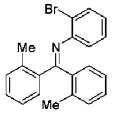
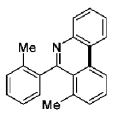
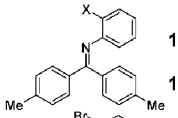
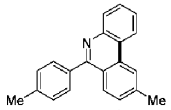
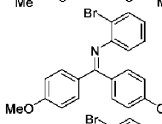
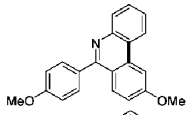
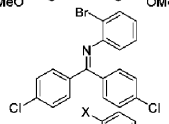
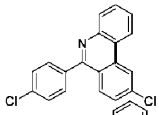
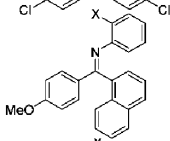
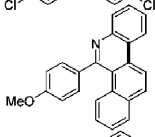
Table 3. Variation of the Imine Derivative[a]

entry	substrate	products/ratio	yield (%)[b]
1	 1e	 2e	94
2	 1f X = Br	 2f	85
3[c]	1f' X = Cl		40
4	 1g	 2g	93
5	 1h	 2h	76
6	 1i X = Br	 2i	89
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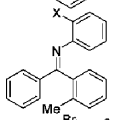
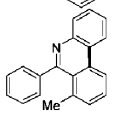
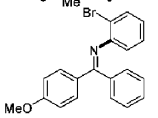
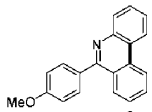
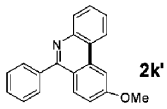
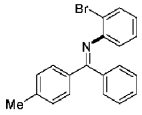
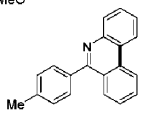
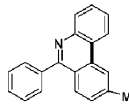
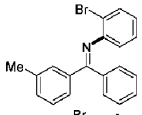
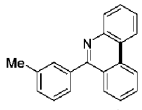
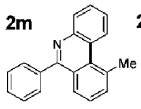
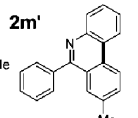
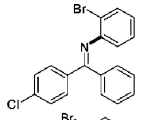
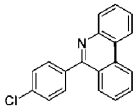
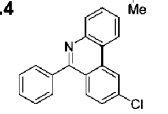
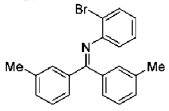
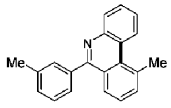
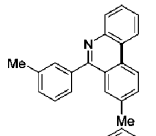
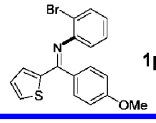
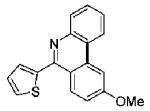
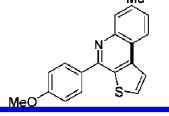
8	 1j X = Br	 2j	77
9[c]	1j' X = Cl		38
10[d]	 1k	 2k 3.7 : 1  2k'	72
11[e]	 1l	 2l 1.3 : 1  2l'	75
12[f]	 1m	 2m  2m'  2m'' 1 : 2 : 1.4	68
13[g]	 1n	 2n 1 : 1.34  2n'	65
14	 1o	 2o 2 : 1  2o'	83
15[h]	 1p	 2p 1 : 4.7  2p'	93

[a]Reaction conditions: *N*-(2-halophenyl)imine **1** (1.0 equiv, 1.0 mmol), Cs_2CO_3 (2.0 equiv), 4 mol % of $Pd(OAc)_2$, 8 mol % of PCy_3, THF (2 mL), 110 °C, 24 h. [b]Yield of isolated product after chromatography. [c]20 mol % 2,2-dimethylpropionic acid was added as additive. [d]The mixed (*E*)/(*Z*) isomers were used in 3.7:1 ratios as substrates. [e](*E*)/(*Z*) = 1.26:1. [f](*E*)/(*Z*) = 1:3.4. [g](*E*)/(*Z*) = 1:1.34. [h](*E*)/(*Z*) = 1:4.65.

1558, 1541, 1474, 1457, 1444, 1362, 772, 766, 751, 727, 701, 683; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.66 (d, 1H, J = 8.0 Hz), 8.50 (d, 1H, J = 8.0 Hz), 8.10−8.06 (m, 2H), 7.85−7.82 (m, 1H), 7.74−7.72 (m, 2H), 7.60−7.51 (m, 5H), 2.6 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 161.2, 143.9, 139.9, 138.9, 133.5, 130.4, 129.9, 129.7, 128.8, 128.7, 128.6, 128.4, 126.6, 124.9, 122.0, 121.7, 121.4, 21.6. HRMS-ESI (m/z): $[M + Na]^+$ calcd for $C_{20}H_{15}NNa$ 292.1102; found 292.1104.

3-Chloro-6-phenylphenanthridine (2c).[2a] White solid: mp 133−134 °C; IR (KBr) ν (cm^{-1}) 3062, 2993, 2926, 1608, 1515, 1494, 1465, 1456, 1354, 1249, 1234, 1174, 1032, 830, 735, 726; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.64 (d, 1H, J = 8.0 Hz), 8.53 (d, 1H, J = 8.0 Hz), 8.25−8.24 (m, 1H), 8.13−8.11 (m, 1H), 7.89−7.85 (m, 1H), 7.74−7.72 (m, 2H), 7.65−7.60 (m, 2H), 7.59−7.54 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 162.4, 144.5, 139.4, 134.4, 133.1, 130.0, 129.7, 129.6, 129.1, 128.9, 128.5, 127.5, 127.4, 125.1, 123.3, 122.2, 122.1. HRMS-

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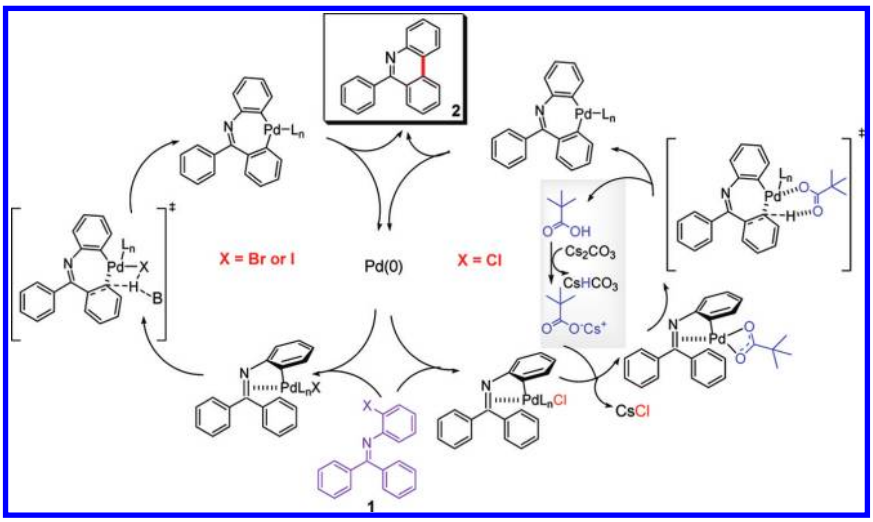
Scheme 1. Proposed Mechanism for the Intramolecular C−H Activation/C−C Bond Formation of *N*-Aryl Imines Using a Palladium Catalyst



ESI (*m*/*z*): [M + Na]$^+$ calcd for $C_{19}H_{12}ClNNa$ 312.0556; found 312.0553.

6-Phenylphenanthridine-2-carbonitrile (2d). White solid: mp 233−234 °C; IR (KBr) ν (cm^{-1}) 3076, 3026, 2922, 2224, 1609, 1560, 1511, 1489, 1442, 1422, 1363, 960, 903, 830, 777, 754, 689, 670, 617; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.95 (m, 1H), 8.66 (d, 1H, J = 8.0 Hz), 8.29 (d, 1H, J = 8.0 Hz), 8.18 (d, 1H, J = 8.0 Hz), 7.97−7.92 (m, 2H), 7.76−7.71 (m, 3H), 7.61−7.57 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 164.3, 145.5, 139.0, 132.4, 131.6, 131.5, 130.4, 129.7, 129.38, 129.37, 128.6, 128.5, 127.8, 125.6, 123.9, 122.2, 119.1, 110.2. HRMS-ESI (*m*/*z*): [M + Na]$^+$ calcd for $C_{20}H_{12}N_2Na$ 303.0898; found 303.0896.

7-Methyl-6-*o*-tolylphenanthridine (2e). Pale yellow solid: mp 149−150 °C; IR (KBr) ν (cm^{-1}) 3055, 3016, 2966, 2929, 2858, 1598, 1565, 1519, 1474, 1458, 1448, 1377, 1330, 1293, 1030, 955, 937, 779, 760, 742, 727; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.66−8.63 (m, 2H), 8.22−8.19 (m, 1H), 7.76−7.66 (m, 3H), 7.43−7.41 (m, 1H), 7.39−7.29 (m, 4H), 2.09 (s, 3H), 2.03 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 160.7, 144.1, 142.9, 137.6, 135.4, 134.4, 131.4, 130.3, 130.2, 129.9, 128.6, 128.5, 128.2, 126.9, 125.9, 125.1, 123.9, 122.2, 120.7, 23.9, 19.7. HRMS-ESI (*m*/*z*): [M + Na]$^+$ calcd for $C_{21}H_{17}NNa$ 306.1259; found 306.1263.

9-Methyl-6-*p*-tolylphenanthridine (2f). Pale yellow solid: mp 77−78 °C; IR (KBr) ν (cm^{-1}) 3067, 3027, 2918, 2855, 1619, 1577, 1561, 1510, 1494, 1458, 1361 1343, 1326, 1183, 1139, 1038, 960, 840, 828, 815, 761, 737; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.59 (d, 1H, J = 8.0 Hz), 8.46 (m, 1H), 8.24 (d, 1H, J = 8.0 Hz), 8.03 (d, 1H, J = 8.0 Hz), 7.76−7.72 (m, 1H), 7.67−7.63 (m, 3H), 7.43−7.37 (m, 3H), 2.64 (s, 3H), 2.49 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 161.1, 144.1, 140.8, 138.5, 137.1, 133.6, 130.2, 129.7, 129.1, 128.8, 128.7, 128.6, 126.5, 123.5, 123.4, 121.9, 121.8, 22.2, 21.4. HRMS-ESI (*m*/*z*): [M + Na]$^+$ calcd for $C_{21}H_{17}NNa$ 306.1259; found 306.1261.

9-Methoxy-6-(4-methoxyphenyl)phenanthridine (2g). White solid: mp 148.5−149.5 °C; IR (KBr) ν (cm^{-1}) 3051, 2958, 2935, 2828, 1615, 1509, 1455, 1362, 1280, 1227, 1171, 1014, 828, 760, 742; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.56−8.54 (m, 1H), 8.24−8.22 (m, 1H), 8.10 (d, 1H, J = 9.2 Hz), 8.03 (m, 1H), 7.78−7.65 (m, 4H), 7.25−7.23 (m, 1H), 7.12−7.10 (m, 2H), 4.09 (s, 3H), 3.94 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 161.2, 160.4, 160.1, 144.3, 135.6, 132.5, 131.1, 130.9, 130.2, 128.8, 126.2, 123.4, 121.9, 120.3, 117.1, 113.8, 102.9, 55.6, 55.4. HRMS-ESI (*m*/*z*): [M + Na]$^+$ calcd for $C_{21}H_{17}NNaO_2$ 338.1157; found 338.1159.

9-Chloro-6-(4-chlorophenyl)phenanthridine (2h).[9f] White solid: mp 218−219 °C; IR (KBr) ν (cm^{-1}) 3045, 3008, 2920, 2851, 1601, 1575, 1559, 1455, 1359, 1089, 1015, 959, 825, 758, 723, 698, 668; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.67−8.66 (m, 1H), 8.55−8.53 (m, 1H), 8.23−8.21 (m, 1H), 8.02−7.99 (m, 1H), 7.82−7.78 (m, 1H), 7.74−7.66 (m, 3H), 7.59−7.54 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 159.4, 144.1, 137.7, 137.3, 135.2, 134.8, 131.1, 130.4, 130.1, 129.6, 128.8, 127.9, 127.4, 123.3, 122.7, 122.1, 122.0. HRMS-ESI (*m*/*z*): [M + Na]$^+$ calcd for $C_{19}H_{11}Cl_2NNa$ 346.0166; found 346.0169.

5-(4-Methoxyphenyl)benzo[*i*]phenanthridine (2i). White solid: mp 207−208 °C; IR (KBr) ν (cm^{-1}) 3052, 3009, 2958, 2935, 2829, 1618, 1575, 1563, 1510, 1496, 1456, 1363, 1281, 1249, 1246, 1227, 1172, 1142, 1040, 1015, 858, 841, 828, 759, 752, 742; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.69−8.67 (m, 2H), 8.29−8.27 (m, 1H), 8.20−8.18 (m, 1H), 7.98−7.95 (m, 2H), 7.83−7.78 (m, 1H), 7.73−7.69 (m, 1H), 7.63−7.59 (m, 2H), 7.55−7.51 (m, 1H), 7.30−7.26 (m, 1H), 7.08−7.06 (m, 2H), 3.94 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 159.9, 158.9, 144.1, 137.1, 134.3, 133.2, 132.2, 130.4, 130.3, 129.8, 128.9, 128.4, 128.3, 126.6, 126.3, 125.7, 123.5, 122.4, 121.5, 119.8, 114.5, 55.4. HRMS-ESI (*m*/*z*): [M + Na]$^+$ calcd for $C_{24}H_{17}NNaO$ 358.1208; found 358.1211.

7-Methyl-6-phenylphenanthridine (2j).[2c] Yellow oil: IR ν (cm^{-1}) 3059, 3024, 2966, 2928, 1599, 1581, 1566, 1474, 1457, 1448, 1379, 1337, 1230, 1154, 1030, 955, 761, 736, 701; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.63−8.61 (m, 2H), 8.24 (d, 1H, J = 8.0 Hz), 7.78−7.70 (m, 2H), 7.68−7.66 (m, 1H), 7.57−7.51 (m, 5H), 7.49−7.45 (m, 1H), 2.12 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 160.7, 144.6, 142.8, 137.6, 134.6, 131.3, 130.1, 129.9, 128.6, 128.5, 128.4, 128.1, 126.8, 124.7, 123.8, 122.2, 120.4, 25.0. HRMS-ESI (*m*/*z*): [M + Na]$^+$ calcd for $C_{20}H_{15}NNa$ 292.1102; found 292.1105.

Mixture of 6-(4-Methoxyphenyl)phenanthridine (2k)[3c] and 9-Methoxy-6-phenyl phenanthridine (2k′).[3c] Inseparable white solid (**2k**:**2k′** = 3.7:1): IR (KBr) ν (cm^{-1}) 3052,

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2958, 2828, 1609, 1510, 1481, 1459, 1361, 1286, 1248, 1172, 1028, 829, 760, 729. **2k** (major): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.73 (d, 1H, J = 8.0 Hz), 8.64 (d, 1H, J = 8.0 Hz), 8.26 (d, 1H, J = 8.0 Hz), 8.20 (d, 1H, J = 8.0 Hz), 7.88 (t, 1H, J = 7.6 Hz), 7.80−7.69 (m, 4H), 7.67−7.63 (m, 1H), 7.13 (d, J = 8.8 Hz, 2H), 3.95 (s, 3H). **2k′** (minor): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.57 (d, 1H, J = 8.0 Hz), 8.26 (d, 1H, J = 8.0 Hz), 8.06−8.04 (m, 2H), 7.80−7.69 (m, 3H), 7.69−7.56 (m, 4H), 7.24 (dd, 1H, J = 2.4, 7.8 Hz), 4.09 (s, 3H). HRMS-ESI (m/z): $[M + Na]^+$ calcd for $C_{20}H_{15}NNaO$ 308.1051; found 308.1053.

Mixture of 6-*p*-Tolylphenanthridine (2l)[3c] and 9-Methyl-6-phenylphenanthridine (2l′). Inseparable yellow oil (**2l**:**2l′** = 1.3:1): IR ν (cm^{-1}) 3064, 3029, 2919, 1616, 1575, 1553, 1513, 1484, 1459, 1443, 1359, 1327, 1296, 1033, 959, 824, 761, 729, 703, 669. **2l**: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.72 (d, 1H, J = 8.4 Hz), 8.63 (d, 1H, J = 8.0 Hz), 8.29−8.26 (m, 1H), 8.17 (d, 1H, J = 8.0 Hz), 7.89−7.85 (m, 1H), 7.81−7.76 (m, 1H), 7.73−7.69 (m, 3H), 7.67−7.61 (m, 1H), 7.41 (d, 2H, J = 8.0 Hz), 2.52 (s, 3H). **2l′**: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.63 (d, 1H, J = 8.0 Hz), 8.51 (s, 1H), 8.29−8.26 (m, 1H), 8.02 (d, 1H, J = 8.0 Hz), 7.81−7.76 (m, 3H), 7.73−7.69 (m, 1H), 7.67−7.55 (m, 3H), 7.46 (dd, 1H, J = 0.8, 8.4 Hz), 2.68 (s, 3H). HRMS-ESI (m/z): $[M + Na]^+$ calcd for $C_{20}H_{15}NNa$ 292.1102; found 292.1105.

Mixture of 6-*m*-Tolylphenanthridine (2m),[4d] 10-Methyl-6-phenylphenanthridine (2m′) and 8-Methyl-6-phenylphenanthridine (2m″).[3c] Inseparable yellow oil (**2m**:**2m′**:**2m″** = 1:2:1.4): IR ν (cm^{-1}) 3060, 2992, 2960, 2919, 2872, 1608, 1581, 1567, 1479, 1458, 1443, 1360, 1326, 762, 727, 702. **2m**: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.25 (d, 1H, J = 8.0 Hz), 8.12 (d, 1H, J = 8.0 Hz), 7.99 (d, 1H, J = 7.6 Hz), 7.85 (m, 1H), 7.78−7.67 (m, 3H), 7.61−7.52 (m, 5H), 2.51 (s, 3H). **2m′**: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.87 (d, 1H, J = 8.2 Hz), 8.61−8.58 (m, 1H), 8.31−8.28 (m, 1H), 7.78−7.67 (m, 4H), 7.61−7.52 (m, 4H), 7.35 (d, 1H, J = 8.0 Hz), 3.18 (s, 3H). **2m″**: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.69 (d, 1H, J = 8.2 Hz), 8.60 (d, 1H, J = 8.0 Hz), 8.30 (d, 1H, J = 8.0 Hz), 7.87 (s, 1H), 7.78−7.67 (m, 5H), 7.61−7.52 (m, 3H), 2.49 (s, 3H). HRMS-ESI (m/z): $[M + Na]^+$ calcd for $C_{20}H_{15}NNa$ 292.1102; found 292.1105.

Mixture of 6-(4-Chlorophenyl)phenanthridine (2n)[2a] and 9-Chloro-6-phenyl phenanthridine (2n′).[2c] **2n** and **2n′** can be separated by column chromatography on silica gel, eluting with 1% ethyl acetate/petroleum ether (**2n**:**2n′** = 1:1.34). **2n**: white solid; mp 148−149 °C; IR (KBr) ν (cm^{-1}) 3070, 3046, 2956, 2923, 2852, 1609, 1592, 1559, 1482, 1395, 1359, 1327, 1090, 1015, 960, 829, 752, 723; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.72 (d, 1H, J = 8.4 Hz), 8.63 (d, 1H, J = 8.0 Hz), 8.23 (d, 1H, J = 8.0 Hz), 8.06 (d, 1H, J = 8.0 Hz), 7.88 (dd, 1H, J = 8.0, 7.2 Hz), 7.79−7.75 (m, 1H), 7.72−7.69 (3H, m), 7.63 (dd, 1H, J = 8.0, 7.2 Hz), 7.55 (d, 2H, J = 8.0 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 159.9, 143.7, 138.2, 134.9, 133.5, 131.1, 130.7, 130.3, 128.9, 128.7, 128.5, 127.2, 127.1, 125.0, 123.7, 122.3, 122.0. HRMS-ESI (m/z): $[M + Na]^+$ calcd for $C_{19}H_{12}ClNNa$ 312.0556; found 312.0557. **2n′**: white solid; mp 123−124 °C; IR (KBr) ν (cm^{-1}) 3057, 3027, 2957, 2924, 2853, 1601, 1561, 1509, 1481, 1457, 1442, 1360, 1289, 1073, 825, 756, 730, 695, 665; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.66 (s, 1H), 8.53 (d, 1H, J = 8.4 Hz), 8.24 (d, 1H, J = 8.0 Hz), 8.05 (d, 1H, J = 8.8 Hz), 7.79 (t, 1H, J = 8.0 Hz), 7.72−7.68 (m, 3H), 7.59−7.53 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 160.7, 144.2, 139.3, 137.1, 134.8, 130.5, 130.4, 129.6, 129.5, 128.9, 128.5, 127.7, 127.2, 123.5, 122.7, 122.0, 121.9. HRMS-ESI (m/z): $[M + Na]^+$ calcd for $C_{19}H_{12}ClNNa$ 312.0556; found 312.0557.

Mixture of 8-Methyl-6-*m*-tolylphenanthridine (2o) and 10-Methyl-6-*m*-tolyl phenanthridine (2o′). Inseparable yellow oil (**2o**:**2o′** = 2:1): IR ν (cm^{-1}) 3058, 2960, 2920, 2872, 1581, 1567, 1527, 1478, 1458, 1437, 1359, 1325, 1296, 820, 789, 762, 729, 709. **2o**: ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.86 (d, 1H, J = 8.0 Hz), 8.57 (d, 1H, J = 8.0 Hz), 8.32 (d, 1H, J = 8.0 Hz), 8.01 (d, 1H, J = 8.0 Hz), 7.69−7.65 (m, 3H), 7.51−7.42 (m, 4H), 3.17 (s, 3H), 2.48 (s, 3H). **2o′**: ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.25 (d, 1H, J = 8.0 Hz), 7.88 (m, 1H), 7.78−7.71 (m, 3H), 7.57−7.54 (m, 1H), 7.51−7.42 (m, 2H), 7.37−7.33 (m, 3H), 2.51 (s, 3H), 2.50 (s, 3H). HRMS-ESI (m/z): $[M + Na]^+$ calcd for $C_{21}H_{17}NNa$ 306.1259; found 306.1261.

Mixture of 9-Methoxy-6-(thiophen-2-yl)-phenanthridine (2p) and 4-(4-Methoxy- phenyl)thieno-[2,3-*c*]quinoline (2p′). Inseparable white solid (**2p**:**2p′** = 1:4.7): IR (KBr) ν (cm^{-1}) 3062, 2993, 2926, 1608, 1515, 1494, 1465, 1456, 1354, 1249, 1234, 1174, 1032, 830, 735, 726. **2p**: ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.52−8.45 (m, 2H), 8.16 (d, 1H, J = 8.0 Hz), 7.99 (m, 1H), 7.74−7.70 (m, 1H), 7.64−7.60 (m, 2H), 7.56−7.54 (m, 1H), 7.27 (m, 1H), 7.24−7.21 (m, 1H), 4.06 (s, 3H). **2p′**: ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.30−8.27 (m, 2H), 8.12 (d, 2H, J = 8.0 Hz), 8.05−8.03 (m, 1H), 7.86 (dd, 1H, J = 8.0, 3.2 Hz), 7.74−7.71 (m, 1H), 7.70−7.64 (m, 1H), 7.13−7.10 (m, 2H), 3.92 (s, 3H). HRMS-ESI (m/z): $[M + Na]^+$ calcd for $C_{18}H_{13}NNaOS$ 314.0616; found 314.0619.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

General experimental methods and ^{1}H and ^{13}C NMR spectra of the products **2a**−**p**. This material is available free of charge via the Internet http://pubs.acs.org.

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