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Palladium(II)-Catalyzed Sequential C−H Arylation/Aerobic Oxidative C−H Amination: One-Pot Synthesis of Benzimidazole-Fused Phenanthridines from 2-Arylbenzimidazoles and Aryl Halides

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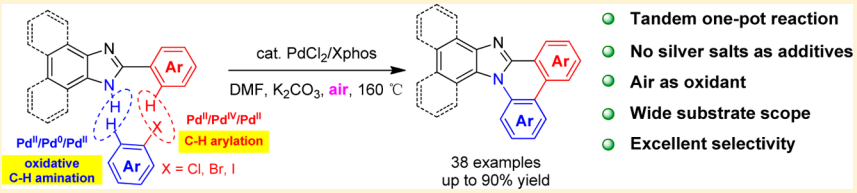
Supporting Information



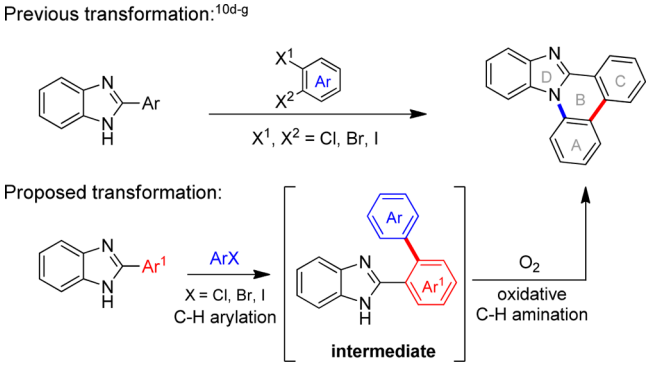
ABSTRACT: Starting from 2-arylbenzimidazoles and aryl halides, an efficient palladium-based catalytic method for the synthesis of benzimidazole-fused phenanthridines has been developed. This reaction sequence comprises intermolecular C−H arylation and intramolecular aerobic oxidative C−H amination, involving the rupture of two C−H bonds, one C−X bond, and one N−H bond in one pot. The Pd^{II}−Pd^{IV}−Pd^{II} and Pd^{II}−Pd^{0}−Pd^{II} catalytic cycles work together under the reported conditions to generate phenanthridines with diverse substituents.

Transition metal-catalyzed direct C−H functionalization has emerged as an attractive strategy for constructing C−C and C−heteroatom bonds in organic synthesis.[1] In particular, directing group-assisted palladium-catalyzed C−H activation has been employed as a powerful method for conducting various different transformations of aromatic compounds.[2] Among these transformations, catalytic direct arylations with aryl(pseudo) halides as electrophilic coupling partners[3] and oxidative C−N cross-coupling reactions[4] have become extraordinarily popular. Despite recent major advancements in chelation-assisted C−C or C−N bond formation, a combination of fundamentally different C−H functionalizations for highly efficient one-pot synthesis of heterocycles is quite challenging, and examples remain scarce.[5,6]

Phenanthridine-fused heterocycles are prevalent in advanced organic materials,[7] biologically and therapeutically active molecules,[8] and significant natural products.[9] Therefore, considerable effort has been focused on straightforward and modular synthetic approaches to (hetero)aryl-fused phenanthridines from simple starting materials.[10] Inspired by Sun's study of benzimidazole-assisted palladium-catalyzed ortho arylation of aromatic C−H bonds,[11] we envisioned that a novel one-pot procedure for the synthesis of benzimidazole-fused phenanthridines from aryl halides was possible through sequential C(sp^2)−H arylation of 2-arylbenzimidazole followed by aerobic oxidative C−H amination (Scheme 1).[12]

To realize this proposed tandem process, we needed to address several issues. First, finding a versatile catalyst system to control chemical selectivity (N-arylation[10d−f,13] vs C-arylation[11]) and accommodate an aerobic oxidative amination step could be a dilemma. Second, more reactive aryl iodides are usually used as arylation reagents in the presence of a stoichiometric amount of silver salts that helped to enhance reactivity and productivity.[5a,c,d,11] Expansion of substrate scope to less reactive aryl bromides and chlorides may be a challenge without the help of copper and silver salt additives.[5a,14]

Scheme 1. One-Pot Synthesis of Benzimidazole-Fused Phenanthridine Derivatives



With these considerations in mind, 2-phenyl benzimidazole (**1a**) and iodobenzene (**2a**) were selected as the coupling partners to verify the assumption mentioned above. Extensive experiments were conducted in the presence of different ligands for the Pd catalyst, bases, solvents, and temperatures using air as the oxidant (Table 1). We first examined the model reaction in DMF at 160 °C for 72 h with $PdCl_2$ as the catalyst and

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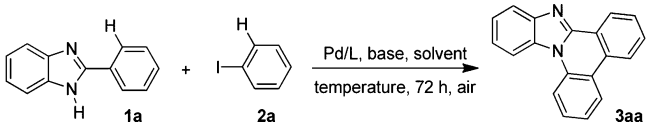
Table 1. Pd-Catalyzed Cascade Annulation Reaction Condition Optimization[a]



1a 2a 3aa

entry	Pd/ligand	base	solvent/temp (°C)	yield (%)[b]
1	$PdCl_2$	K_2CO_3	DMF/160	45
2	$PdCl_2$/dppf	K_2CO_3	DMF/160	26
3	$PdCl_2$/dppe	K_2CO_3	DMF/160	44
4	$PdCl_2$/PCy_3	K_2CO_3	DMF/160	43
5	$PdCl_2$/PPh_3	K_2CO_3	DMF/160	70
6	$PdCl_2$/MePhos	K_2CO_3	DMF/160	78
7	$PdCl_2$/CyJohnPhos	K_2CO_3	DMF/160	75
8	$PdCl_2$/JohnPhos	K_2CO_3	DMF/160	51
9	$PdCl_2$/Xphos	K_2CO_3	DMF/160	90 (67)[c]
10	$PdCl_2$/phenanthroline	K_2CO_3	DMF/160	39
11	$PdCl_2$/2,2′-bipyridine	K_2CO_3	DMF/160	67
12	$Pd_2(dba)_3$/Xphos	K_2CO_3	DMF/160	86
13	$Pd(PPh_3)_4$/Xphos	K_2CO_3	DMF/160	82
14	$Pd(OAc)_2$/Xphos	Cs_2CO_3	DMF/160	92
15	$Pd(OAc)_2$/Xphos	KO^{t}Bu	DMF/160	36
16	$Pd(OAc)_2$/Xphos	Et_3N	DMF/160	0
17	$PdCl_2$/Xphos	K_2CO_3	DMA/160	40
18	$PdCl_2$/Xphos	K_2CO_3	DMSO/160	29
19	$PdCl_2$/Xphos	K_2CO_3	toluene/140	0
20	$PdCl_2$/Xphos	K_2CO_3	THF/100	0
21	$PdCl_2$/Xphos	K_2CO_3	DMF/140	47
22	$PdCl_2$/Xphos	K_2CO_3	DMF/120	trace

[a]Reaction conditions unless otherwise stated: **1a** (0.2 mmol), **2a** (0.6 mmol), base (0.6 mmol), Pd (10 mol %), ligand (20 mol %), solvent (2.0 mL), 72 h, air. [b]Yield of isolated product. [c]A 0.4 mmol portion of **2a** was used.

K_2CO_3 as the base. Fortunately, the desired product **3aa** was obtained in 45% yield (entry 1). Compared to the ligand-free annulation process, the enhancement or inhibition of cascade cross-coupling reactivity was observed in the presence of phosphorus ligands (entries 2−9). It turned out that Buchwald-type ligand Xphos[15] performed best, and the yield was improved to 90% (entry 9). Nitrogen-based ligands[16] usually employed in Pd-catalyzed C−H oxidation reactions were also screened. Traditional ligands such as bipyridine and phenanthroline were inferior to Xphos (entries 10 and 11). The nature of palladium sources and bases influences the efficiency of 2-fold C−H arylation processes. Xphos for $Pd(OAc)_2$ or $PdCl_2$ was found to be the best catalyst system with K_2CO_3 or Cs_2CO_3 as the base (entries 9 and 12−16). Other polar solvents such as *N*,*N*-dimethylacetamide (DMA) and dimethyl sulfoxide (DMSO) were also examined; DMF provided a better result (entries 9, 17, and 18). Nonpolar solvents such as toluene and tetrahydrofuran gave no products (entries 19 and 20). When the reaction temperature was reduced to 140 and 120 °C, the desired annulation product **3aa** was isolated in 47% yield and a trace quantity, respectively (entries 21 and 22, respectively). Changing the quantity of **2a** from 3 to 2 equiv resulted in a smaller yield of 67% (entry 9). In general, Xphos for $Pd(OAc)_2$ or $PdCl_2$ was found to be the best catalyst system with K_2CO_3 or Cs_2CO_3 as the base in DMF at 160 °C.

Having established the feasibility of the tandem C−H arylation/aerobic oxidative C−H amination sequence, we then explored the reaction of various 2-arylbenzo[*d*]imidazoles with aryl iodides to examine the scope and generality of the present annulation process (Scheme 2). Initially, we examined the reaction of iodobenzene with various benzimidazole derivatives (**1a**−**1m** and **1o**−**1w**). Gratifyingly, most of these substrates can be smoothly transformed into (hetero)aryl-fused benzimidazole products **3aa**−**3ma** in moderate to good yields. Benzimidazoles containing electron-donating groups at the para position of the 2-aryl moiety were generally more reactive than those bearing electron-withdrawing substituents and provided higher yields. The incorporation of the sterically hindering methyl group in the ortho and meta positions of the 2-aryl moiety seemed to affect the reaction to some extent, and products **3fa** and **3ga** were afforded in 32 and 44% yields, respectively. In addition, 2-heteroarylbenzimidazoles (**1h** and **1i**), α-naphthyl substrate **1j**, and 2-aryl-1*H*-phenanthro[9,10-*d*]imidazoles (**1l** and **1m**) can also be efficiently transformed into the corresponding products in good yields. However, when the substrate scope is extended to imidazopyridine **1w**, the reaction cannot proceed smoothly to give the corresponding product under the standard conditions [**3wa** (Scheme 2)]. Second, as another reaction partner, aryl iodides (**2b**−**2g**) were then investigated under the optimized conditions. A variety of substituents (such as Me, OMe, F, Ph, and naphthyl) were applicable, and the corresponding products **3ab**−**3ag** can be obtained in good yields. Nevertheless, the reaction of ortho-substituted aryl iodides such as 2-methyl iodobenzene and 2-methoxy iodobenzene gave a complex mixture with a low level of conversion, which is probably the result of the steric hindrance of the ortho substituent.

Regioselectivity issues may potentially exist in this cascade process when asymmetrically substituted 2-aryl benzimidazoles or aryl halides are used. Thus, the regioselectivity of the reaction was then investigated with aryl iodides as arylating reagents (Scheme 3). For substrates **1p**−**1s** bearing substituents at the meta position of the 2-aryl moiety, there are two possible C−H activation sites (C2 and C6), but the arylation process occurred only at the most sterically accessible site, C6, to give single regioisomers (**3pa**−**3sa**). More interestingly, β-naphthyl substrate **1t** also provided a single product **3ta** in 71% yield through β-site specific C−H activation. The complete turnover of site selectivity (α/β) implies that the first direct C−H arylation process is not an outcome of electrophilic aromatic substitutions.[17] 4- or 5-monosubstituted substrates were then investigated to elucidate the influence of the steric effect on the regioselectivity in the Pd-catalyzed oxidative C−N formation step. For 4-methyl-substituted benzimidazoles, oxidative C−H amination occurred specifically at the sterically accessible N atom to give single products **3of** and **3ua** (Scheme 3); however, 5-substituted substrate **1v** gave a 3:1 mixture **3va** in 83% yield. On the other hand, the use of meta-substituted aryl iodides, such as 3-methyl iodobenzene [giving **3ag** (Scheme 2)] and 3-methoxy iodobenzene [giving **3ah** (Scheme 3)], may also lead to regioselectivity preferences in the aerobic oxidative amination step. Similarly, the C−H amination occurred specifically at C6 of meta-substituted aryl iodides in good yields. The C−H amination process at C2 was completely inhibited, probably because of the strong steric repulsion between the meta substituent and the palladium center.

Attempts to extend the substrates from aryl iodides to less reactive aryl bromides and chlorides were then conducted. As shown in Table 2, the present catalytic reaction was compatible with aryl chlorides (entries 1−5) and aryl bromides (entries 6−

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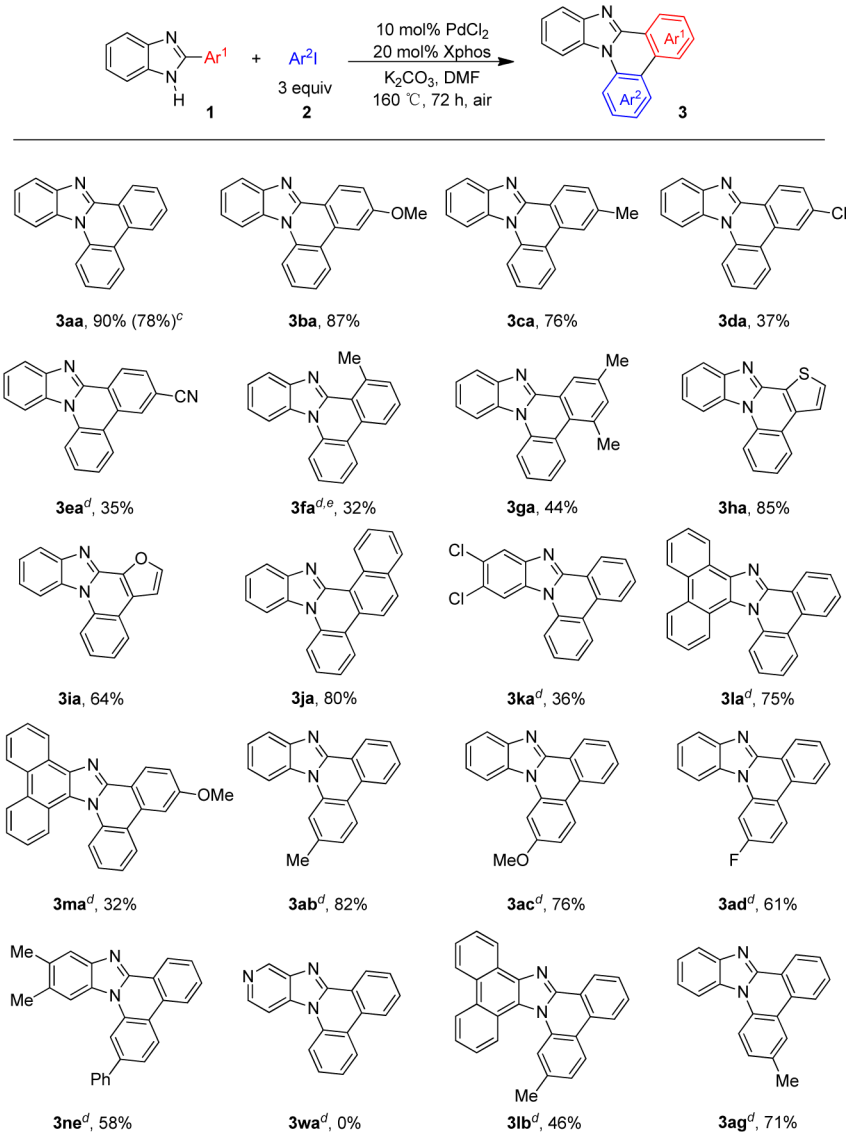
Scheme 2. Pd-Catalyzed Annulation of Benzimidazoles with Aryl Iodides[a,b]



[a]Reaction conditions: **1** (0.2 mmol), **2** (0.6 mmol), K_2CO_3 (0.6 mmol), $PdCl_2$ (0.02 mmol), Xphos (0.04 mmol), DMF (2.0 mL), 160 °C, 72 h, air. [b]Yields of isolated products. [c]The reaction was performed at the 0.5 mmol scale. [d]$Pd(OAc)_2$ was used. [e]Cs_2CO_3 was used.

10), affording the corresponding products in moderate yields. In general, the yield for the aryl halide substrates follows the order aryl iodide > aryl bromide > aryl chloride. The observed trend is consistent with the chemical reactivity of aryl halides.

The reaction of **1a** and 4-methyl iodobenzene **2b** gave **3ab** in 82% yield, and ^1H and ^{13}C NMR spectroscopy data of **3ab** were consistent with the reported literature.[10e] It is important to note that isomer **3ag**, formed probably by Pd-catalyzed tandem N-arylation/oxidative C−C bond formation process, was not observed in the reaction. Consequently, the transformation appears to comprise intermolecular C−H arylation/intramolecular aerobic oxidative C−H amination. To gain further insight into the mechanism of the reaction, the reactivity of two possible intermediates **1x** and **1y** was examined under standard conditions. **1x** can be transformed to **3aa** in 38% yield (eq 1 in Scheme 4); however, for **1y**, the reaction cannot proceed even by using other oxidants[10b] (eq 2 in Scheme 4).

On the basis of the results described above, a possible catalytic cycle is outlined in Scheme 5. The initial step involved the coordination of benzimidazole **1a** to a Pd^{II} species to form **5**, which was followed by an ortho C−H activation to form a five-membered palladacycle **6**. The oxidative addition of **6** by aryl halide **2** gave Pd^{IV} species **7**. Complex **7** underwent C−C reductive elimination to afford ortho-arylated intermediate **8** and a Pd^{II} species. Similarly, **8** was then transformed into a new seven-membered palladacycle **9** through C−H activation. Subsequent K_2CO_3-promoted deprotonation of the N−H group in **9** led to N−Pd bond formation, affording intermediate **10**. Palladacycle **10** underwent C−N reductive elimination to afford the desired product **3aa** and a Pd^0 species, which was oxidized by O_2 to regenerate the active Pd^{II} species[18] for the next catalytic cycle.

In summary, we have developed a Pd(II)-catalyzed 2-fold arylation process via a tandem C−H arylation/aerobic oxidative C−H amination sequence. This method allows the rapid synthesis of diverse heteropolycyclic aromatic compounds from 2-arylbenzimidazoles and aryl halides in good yields with excellent regioselectivities. This Pd(II)-catalyzed tandem

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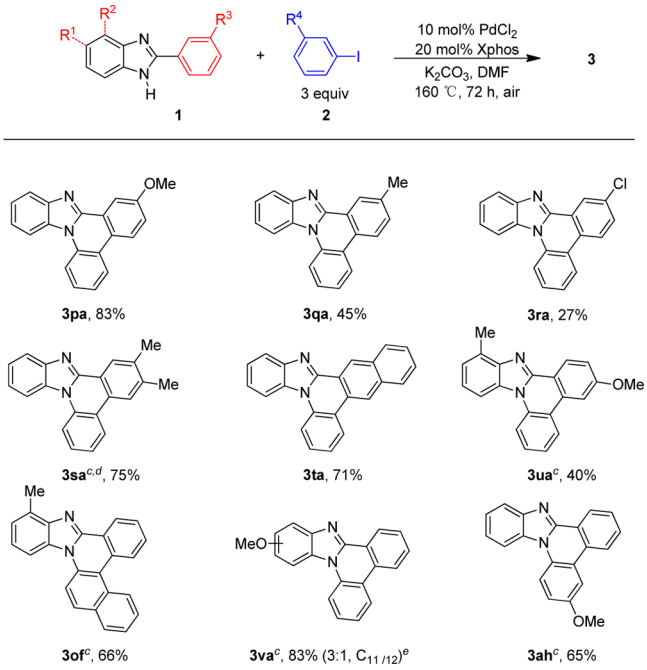
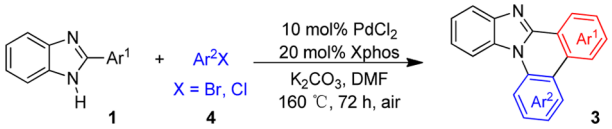
Scheme 3. Regioselectivity of the Pd-Catalyzed Cascade Annulation Reaction[a,b]



[a]Reaction conditions: **1** (0.2 mmol), **2** (0.6 mmol), K_2CO_3 (0.6 mmol), $PdCl_2$ (0.02 mmol), Xphos (0.04 mmol), DMF (2.0 mL), 160 °C, 72 h, air. [b]Yields of isolated products. [c]$Pd(OAc)_2$ was used. [d]Cs_2CO_3 was used. [e]Determined by NMR.

Table 2. Annulation of Benzimidazoles with Aryl Bromides and Chlorides[a]



entry	1	4	product	yield (%)[b]
1	**1a**	PhCl	**3aa**	33
2	**1b**	PhCl	**3ba**	61
3	**1c**	PhCl	**3ca**	44
4	**1j**	PhCl	**3ja**	49
5[c]	**1l**	PhCl	**3la**	56
6	**1a**	PhBr	**3aa**	55
7[c]	**1l**	PhBr	**3la**	61
8[c]	**1a**	*p*-Me-C_6H_4Br	**3ab**	36
9[c]	**1a**	*p*-MeO-C_6H_4Br	**3ac**	45
10[c]	**1a**	*p*-F-C_6H_4Br	**3ad**	30

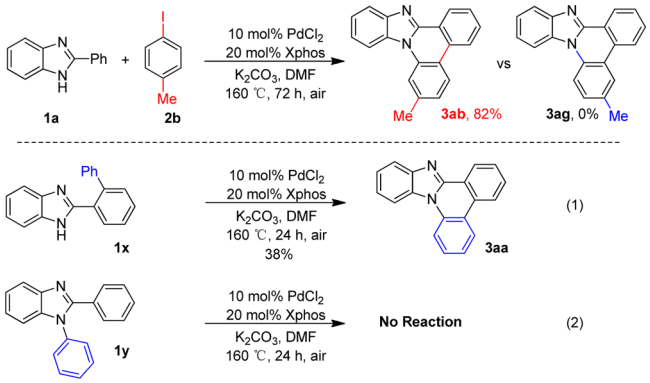
[a]Reaction conditions: benzimidazoles **1** (0.2 mmol), aryl bromides or chlorides **4** (0.6 mmol), K_2CO_3 (0.6 mmol), $PdCl_2$ (0.02 mmol), Xphos (0.04 mmol), DMF (2.0 mL), 160 °C, 72 h, air. [b]Yields of isolated products. [c]$Pd(OAc)_2$ was used.

double arylation will provide a useful tool for the discovery of fluorescent materials and drugs.

EXPERIMENTAL SECTION

General Methods. Chemicals were all purchased from commercial supplies and used without further purification unless otherwise stated. Solvents were dried and purified according to the standard procedures before use. Reactions were monitored by TLC. 2-Aryl benzimidazoles (**1a**−**1k** and **1n**−**1x**),[19] 2-aryl-1*H*-phenanthro[9,10-*d*]imidazoles (**1l** and **1m**),[20] and 1,2-diphenyl-1*H*-benzo[d]imidazole **1y**[21] were

Scheme 4. Investigation of the Reaction Mechanism



prepared according to the literature methods. All reactions were conducted in dried glassware. Melting points were determined on a melting point apparatus in open capillaries and are uncorrected. ^1H NMR spectra were recorded on a 400 MHz spectrometer, and ^{13}C NMR spectra were recorded at 100 MHz. Unless otherwise stated, deuterochloroform ($CDCl_3$) was used as a solvent. Chemical shifts (δ) are given in parts per million downfield relative to tetramethylsilane (TMS, 0.00 ppm). The splitting patterns are reported as s (singlet), d (doublet), dd (double doublet), t (triplet), and m (multiplet). Coupling constants are given in hertz. High-resolution mass spectra were recorded on a BIO TOF Q mass spectrometer.

General Procedures for One-Pot Synthesis of Benzimidazole-Fused Phenanthridines. A 25 mL Schlenk tube equipped with a magnetic stirring bar was charged with 2-arylbenzimidazoles (0.2 mmol, 1.0 equiv), aryl halides (0.6 mmol, 3.0 equiv), and K_2CO_3 (82.5 mg, 0.6 mmol, 3.0 equiv), and then $PdCl_2$ (0.02 mmol, 3.5 mg) or $Pd(OAc)_2$ (0.02 mmol, 4.6 mg) and Xphos (0.04 mmol, 19 mg) were added. Finally, DMF (2.0 mL) was added to the mixture via syringe at room temperature under air. The tube was sealed and put into a preheated oil bath at 160 °C for 72 h. The mixture was cooled to room temperature, quenched with water (5 mL), and diluted with ethyl acetate (8 mL). The layers were separated, and the aqueous layer was extracted with 2 × 8 mL of ethyl acetate. The combined organic extracts were dried over anhydrous sodium sulfate, filtered, and concentrated in vacuo. The crude product was then purified by flash chromatography on silica gel (H), eluting with 3−10% ethyl acetate/petroleum ether.

Benzo[4,5]imidazo[1,2-*f*]phenanthridine (3aa). Pale yellow solid. Mp: 145−147 °C (Lit.[10e,f] mp 144−146 °C). Yield: 90% (48.3 mg). ^1H NMR ($CDCl_3$, 400 MHz): δ 8.62 (1H, d, J = 8.0 Hz), 8.08 (1H, d, J = 8.0 Hz), 8.00−7.91 (4H, m), 7.46 (2H, d, J = 7.2 Hz), 7.39 (1H, t, J = 8.0 Hz), 7.29 (2H, m), 7.12−7.10 (1H, m). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 147.2, 144.3, 134.1, 131.7, 130.2, 129.2, 128.8, 128.4, 125.8, 124.1, 124.0, 123.8, 123.2, 122.7, 122.0, 121.3, 120.2, 115.7, 113.8.

2-Methyl-benzo[4,5]imidazo[1,2-*f*]phenanthridine (3ab). White solid. Mp: 184−186 °C (Lit.[10e] mp 187−189 °C). Yield: 82% (46.3 mg). ^1H NMR ($CDCl_3$, 400 MHz): δ 8.75−8.73 (1H, m), 8.14 (1H, d, J = 8.0 Hz), 8.10 (1H, d, J = 8.0 Hz), 8.05 (1H, s), 8.04 (1H, d, J = 8.0 Hz), 8.00 (1H, d, J = 8.0 Hz), 7.61−7.53 (2H, m), 7.48−7.44 (1H, m), 7.41−7.37 (1H, m), 7.06 (1H, d, J = 8.0 Hz), 2.43 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 147.8, 144.6, 134.5, 132.3, 131.9, 130.9, 130.4, 129.7, 128.2, 126.1, 125.6, 124.1, 123.1, 122.8, 122.0, 120.4, 119.3, 116.3, 114.0, 22.0.

2-Methoxy-benzo[4,5]imidazo[1,2-*f*]phenanthridine (3ac). White solid. Mp: 217−219 °C (Lit.[10e] mp 219−221 °C). Yield: 76% (45.3 mg). ^1H NMR ($CDCl_3$, 400 MHz): δ 8.83 (1H, d, J = 8.0 Hz), 8.35 (1H, d, J = 9.2 Hz), 8.29−8.27 (2H, m), 8.06−8.01 (2H, m), 7.69 (1H, m), 7.61 (1H, m), 7.52−7.46 (2H, m), 7.05 (1H, d, J = 8.0 Hz), 4.02 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 160.3, 147.9, 144.6, 135.5, 131.7, 130.4, 129.7, 127.5, 126.0, 125.4, 124.1, 122.7, 122.2, 121.6, 120.3, 115.0, 113.7, 110.8, 101.3, 55.6.

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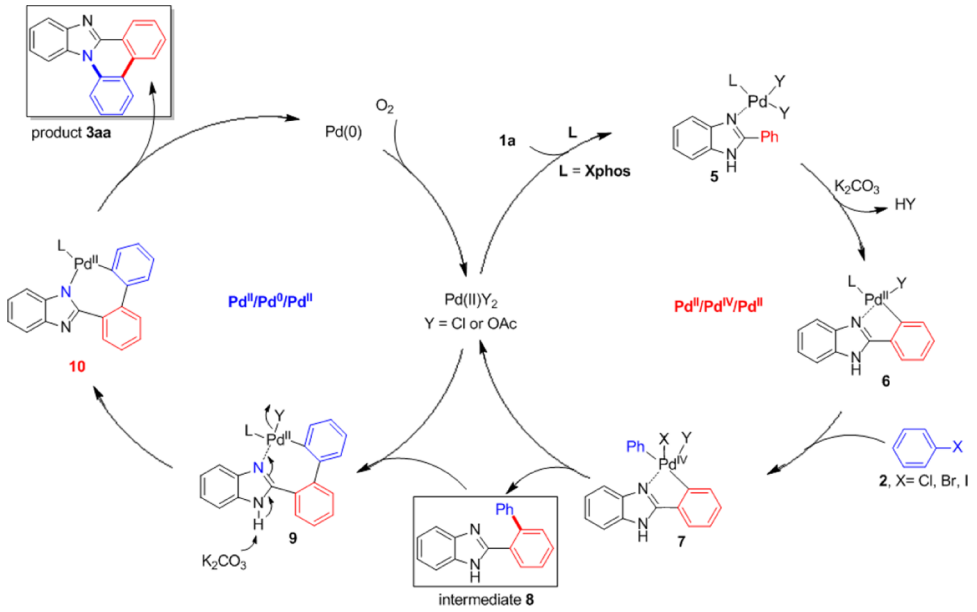
Scheme 5. Proposed Catalytic Pathway



2-Fluoro-benzo[4,5]imidazo[1,2-*f*]phenanthridine (3ad). White solid. Mp: 168−169 °C. Yield: 61% (35 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.80 (1H, d, J = 8.0 Hz), 8.37 (1H, t, J = 8.0 Hz), 8.23−8.15 (3H, m), 8.03 (1H, d, J = 8.0 Hz), 7.71−7.61 (2H, m), 7.54−7.46 (2H, m), 7.18 (1H, t, J = 8.0 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 162.6 (d, J = 167 Hz), 147.4, 144.4, 135.0, 131.7, 130.7, 128.9, 128.4, 126.0, 125.9 (d, J = 7 Hz), 124.4, 123.2, 122.8, 122.0, 120.5, 118.0 (d, J = 3 Hz), 113.5, 112.0 (d, J = 15 Hz), 103.2 (d, J = 18 Hz). HRMS-ESI: [M + Na]$^+$ calcd for $C_{19}H_{11}FN_2Na$ m/z 309.0804, found m/z 309.0806.

11,12-Dimethyl-2-phenyl-benzo[4,5]imidazo[1,2-*f*]-phenanthridine (3ne). White solid. Mp: 246−248 °C. Yield: 58% (43.2 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.85 (1H, dd, J = 8.0, 1.2 Hz), 8.74 (1H, d, J = 1.2 Hz), 8.52 (1H, d, J = 8.4 Hz), 8.38 (1H, d, J = 8.0 Hz), 8.12 (1H, s), 7.81−7.79 (3H, m), 7.74−7.70 (3H, m), 7.68−7.64 (3H, m), 2.53 (3H, s), 2.48 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 147.1, 143.2, 142.1, 140.4, 135.0, 133.3, 132.2, 130.4, 130.1, 129.2, 128.5, 128.1, 127.5, 127.4, 127.0, 125.9, 124.6, 123.2, 122.3, 120.7, 120.4, 114.4, 114.2, 21.2, 20.4. HRMS-ESI: [M + Na]$^+$ calcd for $C_{27}H_{20}N_2Na$ m/z 395.1524, found m/z 395.1527.

10-Methyl-benzo[*a*]benzo[4,5]imidazo[1,2-*f*]-phenanthridine (3of). White solid. Mp: 193−195 °C. Yield: 66% (43.8 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 9.03 (1H, dd, J = 7.2, 1.6 Hz), 8.90 (1H, d, J = 8.4 Hz), 8.76 (1H, dd, J = 8.4, 1.2 Hz), 8.69 (1H, d, J = 9.2 Hz), 8.22 (1H, d, J = 8.0 Hz), 8.07 (1H, d, J = 8.8 Hz), 8.00 (1H, d, J = 8.0 Hz), 7.74−7.64 (3H, m), 7.57 (1H, d, J = 7.6 Hz), 7.39−7.32 (2H, m), 2.89 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 147.0, 144.2, 133.1, 131.4, 131.3, 130.5, 130.3, 129.8, 129.5, 129.3, 128.6, 127.9, 127.8, 127.2, 127.0, 126.3, 125.4, 124.6, 124.5, 122.5, 117.1, 115.1, 111.5, 17.2. HRMS-ESI: [M + Na]$^+$ calcd for $C_{24}H_{16}N_2Na$ m/z 355.1211, found m/z 355.1213.

3-Methyl-benzo[4,5]imidazo[1,2-*f*]phenanthridine (3ag). White solid. Mp: 201−202 °C. Yield: 71% (40.1 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.85 (1H, d, J = 8.0 Hz), 8.39−8.25 (3H, m), 8.20−8.17 (1H, m), 8.04 (1H, d, J = 8.0 Hz), 7.72−7.65 (2H, m), 7.52−7.40 (3H, m), 2.52 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 147.4, 144.5, 134.0, 132.3, 131.8, 130.3, 130.0, 129.4, 128.4, 126.0, 124.2, 123.9, 123.4, 122.7, 122.2, 121.5, 120.3, 115.7, 113.8, 21.3. HRMS-ESI: [M + Na]$^+$ calcd for $C_{20}H_{14}N_2Na$ m/z 305.1055, found m/z 305.1057.

3-Methoxy-benzo[4,5]imidazo[1,2-*f*]phenanthridine (3ah). White solid. Mp: 180−182 °C. Yield: 65% (38.7 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.82 (1H, d, J = 7.2 Hz), 8.37 (1H, d, J = 8.0 Hz), 8.22−8.20 (2H, m), 8.03 (1H, d, J = 8.0 Hz), 7.79 (1H, s), 7.69−7.62 (2H, m), 7.49 (1H, t, J = 8.0 Hz), 7.43 (1H, t, J = 8.0 Hz), 7.16 (1H, d, J = 8.0 Hz), 3.92 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 156.0, 147.0, 144.3, 131.6, 130.2, 129.1, 128.6, 128.5, 126.0, 123.8, 123.6, 122.9, 122.7, 122.2, 120.2, 116.9, 115.7, 113.5, 107.8, 55.6. HRMS-ESI: [M + Na]$^+$ calcd for $C_{20}H_{14}N_2NaO$ m/z 321.1004, found m/z 321.1006.

6-Methoxy-benzo[4,5]imidazo[1,2-*f*]phenanthridine (3ba). White solid. Mp: 170−171 °C (Lit.[10e−g] mp 172−174 °C). Yield: 87% (51.9 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.67 (1H, d, J = 8.8 Hz), 8.36 (1H, d, J = 8.4 Hz), 8.18 (2H, d, J = 8.0 Hz), 7.96 (1H, d, J = 7.6 Hz), 7.56−7.51 (2H, m), 7.46 (1H, t, J = 8.0 Hz), 7.41−7.36 (1H, m), 7.32 (1H, t, J = 8.0 Hz), 7.16 (1H, dd, J = 8.8, 2.4 Hz), 3.92 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 161.3, 147.6, 144.6, 134.5, 131.7, 131.1, 129.1, 127.7, 124.1, 124.0, 123.9, 122.3, 121.2, 121.5, 119.9, 116.4, 115.8, 113.7, 105.3, 55.4.

6-Methyl-benzo[4,5]imidazo[1,2-*f*]phenanthridine (3ca). White solid. Mp: 156−157 °C (Lit.[10f,g] mp 156−157 °C). Yield: 76% (42.9 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.67 (1H, d, J = 8.4 Hz), 8.42 (1H, d, J = 8.0 Hz), 8.32 (1H, d, J = 7.6 Hz), 8.24 (1H, d, J = 8.0 Hz), 8.02−7.99 (2H, m), 7.59−7.55 (1H, m), 7.50−7.35 (4H, m), 2.53 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 147.7, 144.6, 140.6, 134.4, 131.8, 129.9, 129.4, 128.9, 125.9, 124.2, 124.0, 123.9, 122.6, 122.2, 121.5, 121.0, 120.1, 115.8, 113.8, 22.1.

6-Chloro-benzo[4,5]imidazo[1,2-*f*]phenanthridine (3da). Pale yellow solid. Mp: 197−198 °C (Lit.[10e−g] mp 198−200 °C). Yield: 37% (22.4 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.75 (1H, d, J = 8.4 Hz), 8.50 (1H, d, J = 8.4 Hz), 8.35−8.28 (3H, m), 8.01 (1H, d, J = 8.0 Hz), 7.69 (1H, quint, J = 8.0, 3.2 Hz), 7.60 (1H, d, J = 8.8 Hz), 7.53−7.45 (3H, m). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 146.7, 144.5, 136.8, 134.7, 131.7, 130.8, 129.8, 128.9, 127.5, 124.5, 124.31, 124.30, 123.2, 122.2, 121.8, 120.5, 120.4, 116.1, 113.9.

Benzo[4,5]imidazo[1,2-*f*]phenanthridine-6-carbonitrile (3ea). Pale yellow solid. Mp: 256−258 °C (Lit.[10e,g] mp 258−260 °C). Yield: 35% (20.5 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.92 (1H, d, J = 8.0 Hz), 8.62 (1H, s), 8.56 (1H, d, J = 8.0 Hz), 8.40 (1H, d, J = 8.0 Hz), 8.34 (1H, d, J = 8.0 Hz), 8.06 (1H, d, J = 8.0 Hz), 7.85 (1H, d, J = 8.0 Hz), 7.77 (1H, t, J = 8.0 Hz), 7.57−7.52 (3H, m). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 145.6, 144.5, 134.7, 131.8, 130.6, 130.5, 129.7, 127.1, 126.9, 126.4, 125.0, 124.8, 124.4, 124.1, 121.0, 120.1, 118.6, 116.2, 114.1, 113.7.

8-Methyl-benzo[4,5]imidazo[1,2-*f*]phenanthridine (3fa). White solid. Mp: 141−142 °C (Lit.[10g] mp 141−142 °C). Yield: 32% (18.1 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.62−8.18 (4H, m), 7.85−7.40 (7H, m), 3.39 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 148.0,

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144.5, 139.6, 134.4, 131.7, 130.8, 130.7, 129.2, 128.8, 124.5, 124.2, 123.6, 122.9, 122.4, 122.2, 120.7, 120.1, 115.6, 113.8, 25.3.

8-Methyl-benzo[4,5]imidazo[1,2-*f*]phenanthridine (3ga). White solid. Mp: 188−189 °C. Yield: 44% (26.1 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.63 (1H, s), 8.56−8.51 (2H, m), 8.29 (1H, dd, J = 7.2, 1.6 Hz), 8.01 (1H, d, J = 8.0 Hz), 7.63−7.58 (1H, m), 7.51−7.39 (3H, m), 7.35 (1H, s), 2.93 (3H, s), 2.51 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 148.4, 144.8, 137.9, 136.4, 134.8, 134.3, 131.7, 128.4, 127.9, 126.7, 124.8, 124.3, 124.0, 123.5, 123.2, 122.6, 120.2, 115.8, 113.9, 25.9, 20.9. HRMS-ESI: $[M + Na]^+$ calcd for $C_{21}H_{16}N_2Na$ m/z 319.1211, found m/z 319.1213.

Benzo[4,5]imidazo[1,2-*a*]thieno[2,3-*c*]quinoline (3ha). Pale yellow solid. Mp: 187−188 °C (Lit.[10e,f] mp 190−194 °C). Yield: 85% (46.6 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.59 (1H, d, J = 8.0 Hz), 8.35 (1H, d, J = 8.0 Hz), 8.18 (1H, d, J = 8.0 Hz), 8.03 (1H, d, J = 8.0 Hz), 7.81−7.80 (1H, m), 7.72−7.66 (2H, m), 7.54−7.45 (3H, m). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 144.9, 144.7, 137.3, 134.2, 131.4, 129.9, 128.4, 126.6, 125.2, 124.3, 122.7, 122.5, 120.5, 120.2, 115.9, 113.8.

Benzo[4,5]imidazo[1,2-*a*]furo[2,3-*c*]quinoline (3ia). Pale yellow solid. Mp: 156−157 °C (Lit.[10g] mp 156−157 °C). Yield: 64% (33 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.64 (1H, d, J = 8.0 Hz), 8.39 (1H, d, J = 8.0 Hz), 8.06 (2H, d, J = 8.0 Hz), 7.90 (1H, m), 7.70 (1H, m), 7.54−7.49 (3H, m), 7.19 (1H, m). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 146.9, 144.8, 141.0, 140.3, 133.9, 131.4, 127.9, 125.1, 124.4, 124.3, 123.9, 122.8, 120.7, 118.8, 115.9, 113.7, 106.2.

Benzo[*i*]benzo[4,5]imidazo[1,2-*f*]phenanthridine (3ja). White solid. Mp: 237−238 °C (Lit.[10g] mp 237−238 °C). Yield: 80% (50.9 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 11.02 (1H, d, J = 8.4 Hz), 8.72 (1H, dd, J = 7.6, 0.8 Hz), 8.65 (1H, dd, J = 8.4, 1.2 Hz), 8.51 (1H, d, J = 9.2 Hz), 8.47 (1H, d, J = 8.0 Hz), 8.20 (1H, dd, J = 7.2, 1.2 Hz), 8.16 (1H, d, J = 8.8 Hz), 8.00 (1H, d, J = 7.6 Hz), 7.93−7.89 (1H, m), 7.80−7.76 (1H, m), 7.73−7.69 (1H, m), 7.61−7.52 (3H, m). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 147.6, 144.7, 134.5, 133.3, 131.6, 130.8, 130.7, 129.4, 129.2, 128.4, 128.2, 127.0, 124.9, 124.3, 124.1, 123.0, 121.9, 120.8, 119.7, 118.9, 115.7, 114.0.

11,12-Dichloro-benzo[4,5]imidazo[1,2-*f*]phenanthridine (3ka). White solid. Mp: 231−232 °C (Lit.[10g] mp 231−232 °C). Yield: 36% (24.2 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.77 (1H, dd, J = 8.0, 1.2 Hz), 8.47 (1H, dd, J = 8.0, 1.2 Hz), 8.38 (1H, s), 8.36 (1H, d, J = 8.4 Hz), 8.31 (1H, d, J = 8.4 Hz), 8.04 (1H, s), 7.78−7.66 (3H, m), 7.54 (1H, t, J = 8.0 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 149.1, 144.0, 133.6, 131.1, 130.8, 129.7, 129.5, 128.8, 128.2, 126.5, 126.2, 125.1, 124.4, 122.9, 122.4, 121.8, 121.1, 115.7, 115.1.

Phenanthro[9,10-*d*]imidazo[1,2-*f*]phenanthridine (3la). White solid. Mp: 293−294 °C. Yield: 75% (55.2 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.96−8.91 (2H, m), 8.80 (1H, d, J = 8.4 Hz), 8.73 (1H, d, J = 8.0 Hz), 8.47−8.40 (4H, m), 7.77 (1H, t, J = 7.6 Hz), 7.73−7.69 (3H, m), 7.64−7.54 (4H, m). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 147.8, 141.5, 133.6, 129.7, 129.6, 129.4, 129.0, 128.7, 127.4, 127.2, 127.1, 126.4, 125.5, 125.4, 125.2, 125.1, 124.7, 124.6, 124.2, 124.1, 123.8, 123.4, 123.2, 123.1, 123.0, 122.3, 119.5. HRMS-ESI: $[M + Na]^+$ calcd for $C_{27}H_{16}N_2Na$ m/z 391.1211, found m/z 391.1214.

6-Methoxy-phenanthro[9,10-*d*]imidazo[1,2-*f*]-phenanthridine (3ma). White solid. Mp: 160−162 °C. Yield: 32% (25.5 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.89 (1H, d, J = 8.0 Hz), 8.77 (2H, d, J = 8.0 Hz), 8.71 (1H, d, J = 8.0 Hz), 8.39 (1H, d, J = 8.0 Hz), 8.34−8.29 (2H, m), 7.77−7.66 (3H, m), 7.59−7.44 (4H, m), 7.23 (1H, d, J = 8.0 Hz), 3.98 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 161.0, 148.0, 141.3, 133.8, 131.2, 129.6, 128.8, 127.4, 127.3, 127.2, 127.0, 126.4, 125.3, 125.1, 124.8, 124.7, 124.6, 123.9, 123.7, 123.4, 123.0, 122.9, 122.8, 119.6, 117.8, 116.6, 105.6, 55.6. HRMS-ESI: $[M + Na]^+$ calcd for $C_{28}H_{18}N_2NaO$ m/z 421.1317, found m/z 421.1318.

2-Methyl-phenanthro[9,10-*d*]imidazo[1,2-*f*]phenanthridine (3lb). White solid. Mp: 258−260 °C. Yield: 46% (35.2 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.97 (1H, d, J = 8.0 Hz), 8.94−8.92 (1H, m), 8.83 (1H, d, J = 8.4 Hz), 8.76 (1H, d, J = 8.4 Hz), 8.50 (1H, d, J = 8.0 Hz), 8.39−8.37 (1H, m), 8.33 (1H, d, J = 8.0 Hz), 8.26 (1H, s), 7.80 (1H, t, J = 7.2 Hz), 7.75−7.69 (3H, m), 7.67−7.57 (2H, m), 7.36 (1H, d, J = 8.0 Hz), 2.53 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz): δ147.9, 141.4, 137.7, 133.5, 129.7, 129.5, 129.0, 128.2, 127.4, 127.2, 126.4, 125.5, 125.2, 125.0, 124.5, 124.4, 124.0, 123.9, 123.8, 123.4, 123.2, 123.0, 122.0, 120.6, 119.8, 21.5. HRMS-ESI: $[M + Na]^+$ calcd for $C_{28}H_{18}N_2Na$ m/z 405.1368, found m/z 405.1371.

7-Methoxy-benzo[4,5]imidazo[1,2-*f*]phenanthridine (3pa). White solid. Mp: 168−169 °C (Lit.[10e,g] mp 163−165 °C). Yield: 83% (49.5 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.30 (1H, d, J = 8.0 Hz), 8.18 (1H, d, J = 8.0 Hz), 8.10 (1H, d, J = 8.0 Hz), 8.07 (1H, m), 8.00 (2H, t, J = 8.0 Hz), 7.48−7.37 (3H, m), 7.27 (1H, t, J = 8.0 Hz), 7.14 (1H, dd, J = 8.0, 4.0 Hz), 3.97 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 159.7, 147.1, 144.3, 133.2, 131.8, 127.7, 124.5, 124.1, 123.9, 123.8, 123.3, 122.9, 122.7, 121.5, 120.2, 120.1, 115.6, 113.9, 106.2, 55.8.

7-Methyl-benzo[4,5]imidazo[1,2-*f*]phenanthridine (3qa). Pale yellow solid. Mp: 158−159 °C (Lit.[10g] mp 158−159 °C). Yield: 45% (25.4 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.60 (1H, s), 8.45−8.41 (1H, m), 8.31−8.24 (2H, m), 8.14−8.11 (1H, m), 8.01 (1H, d, J = 8.0 Hz), 7.59−7.54 (1H, m), 7.51−7.37 (4H, m), 2.53 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 147.5, 144.5, 138.8, 134.0, 131.9, 131.7, 128.5, 127.0, 125.7, 124.3, 124.0, 123.9, 123.2, 122.7, 122.2, 121.7, 120.3, 115.8, 113.9, 21.3.

7-Chloro-benzo[4,5]imidazo[1,2-*f*]phenanthridine (3ra). White solid. Mp: 216−217 °C (Lit.[10g] mp 216−217 °C). Yield: 27% (16.3 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.78 (1H, s), 8.46 (1H, d, J = 8.0 Hz), 8.32−8.26 (2H, m), 8.19 (1H, d, J = 8.0 Hz), 8.01 (1H, d, J = 8.0 Hz), 7.67−7.58 (2H, m), 7.54−7.42 (3H, m). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 146.4, 144.7, 135.0, 134.5, 132.1, 130.9, 129.7, 128.0, 125.7, 124.9, 124.8, 124.7, 124.4, 124.2, 123.6, 121.1, 120.8, 116.3, 114.3.

6,7-Dimethyl-benzo[4,5]imidazo[1,2-*f*]phenanthridine (3sa). White solid. Mp: 177−178 °C. Yield: 75% (44.4 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.50 (1H, m), 8.45−8.38 (1H, m), 8.31−8.25 (2H, m), 8.00 (1H, d, J = 8.0 Hz), 7.97−7.91 (1H, m), 7.55−7.34 (4H, m), 2.41 (6H, s). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 147.6, 144.5, 139.8, 138.0, 134.1, 131.8, 128.3, 127.3, 126.1, 124.1, 123.9, 123.7, 122.7, 122.4, 121.6, 121.1, 120.1, 115.8, 113.8, 20.6, 19.7. HRMS-ESI: $[M + Na]^+$ calcd for $C_{21}H_{16}N_2Na$ m/z 319.1211, found m/z 319.1213.

Benzo[*j*]benzo[4,5]imidazo[1,2-*f*]phenanthridine (3ta). White yellow solid. Mp: 240−241 °C. Yield: 71% (45.2 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 9.14 (1H, s), 8.46 (1H, s), 8.29 (1H, d, J = 8.0 Hz), 8.22 (1H, d, J = 8.0 Hz), 8.09 (1H, d, J = 8.0 Hz), 7.97−7.93 (2H, m), 7.81 (1H, d, J = 4.0 Hz), 7.47−7.42 (4H, m), 7.37 (1H, t, J = 8.0 Hz), 7.28 (1H, t, J = 8.0 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 147.8, 144.6, 134.4, 133.9, 132.8, 132.2, 129.1, 128.6, 128.3, 127.5, 126.9, 126.7, 125.8, 124.6, 124.4, 124.0, 123.1, 122.0, 121.4, 120.3, 116.1, 113.8. HRMS-ESI: $[M + Na]^+$ calcd for $C_{23}H_{14}N_2Na$ m/z 341.1055, found m/z 341.1057.

10-Methyl-6-methoxy-benzo[4,5]imidazo[1,2-*f*]-phenanthridine (3ua). White solid. Mp: 176−177 °C. Yield: 40% (25 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.79 (1H, d, J = 8.0 Hz), 8.49 (1H, d, J = 8.0 Hz), 8.33 (1H, d, J = 8.0 Hz), 8.09 (1H, d, J = 8.0 Hz), 7.69 (1H, s), 7.63 (1H, t, J = 8.0 Hz), 7.42 (1H, t, J = 8.0 Hz), 7.32−7.20 (3H, m), 3.97 (3H, s), 2.83 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 161.3, 147.0, 143.9, 134.8, 131.4, 131.0, 129.9, 129.1, 128.0, 124.2, 124.1, 124.0, 122.2, 121.5, 117.3, 116.4, 116.0, 111.2, 105.3, 55.5, 17.0. HRMS-ESI: $[M + Na]^+$ calcd for $C_{21}H_{16}N_2NaO$ m/z 335.1160, found m/z 335.1161.

Mixture of 11-Methoxy-benzo[4,5]imidazo[1,2-*f*]-phenanthridine and 12-Methoxy-benzo[4,5]imidazo[1,2-*f*]-phenanthridine (3va). Inseparable pale yellow solid (3:1). Mp: 138−142 °C. Yield: 83% (49.5 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.84 (0.3H, d, J = 8.0 Hz), 8.80 (1H, d, J = 8.0 Hz), 8.47 (0.3H, d, J = 8.0 Hz), 8.45−8.43 (2.3H, m), 8.38−8.33 (1.3H, m), 8.19 (0.3H, d, J = 8.0 Hz), 7.93 (1H, d, J = 8.0 Hz), 7.80 (1H, s), 7.71−7.63 (3.9H, m), 7.50−7.46 (1.6H, m), 7.17 (1H, d, J = 8.0 Hz), 7.09 (0.3H, d, J = 8.0 Hz), 4.00 (3H, s), 3.96 (1H, s). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 157.3, 156.6, 148.0, 147.2, 145.9, 139.3, 134.6, 134.4, 132.4, 130.4, 130.2, 129.5, 129.3, 129.2, 128.8, 128.7, 126.5, 126.0, 125.8, 124.5, 124.4, 123.9, 123.5, 122.4, 122.0, 121.7, 120.7, 115.9, 114.5, 112.9,

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112.6, 102.1, 99.0, 56.4, 55.8. HRMS-ESI: $[M + Na]^+$ calcd for $C_{20}H_{14}N_2NaO$ m/z 321.1004, found m/z 321.1005.

■ ASSOCIATED CONTENT

Supporting Information

^1H and ^{13}C NMR spectra of the products. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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