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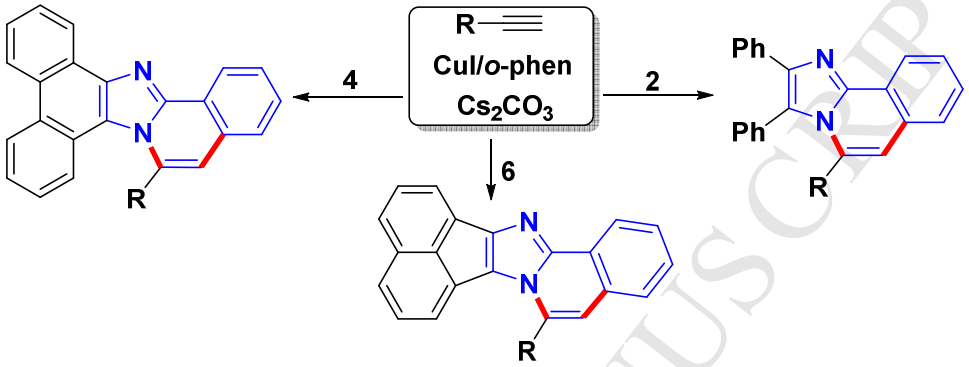

CuI-catalyzed Sonogashira Reaction for the Efficient Synthesis of 1*H*-Imidazo[2,1-*a*]isoquinoline Derivatives

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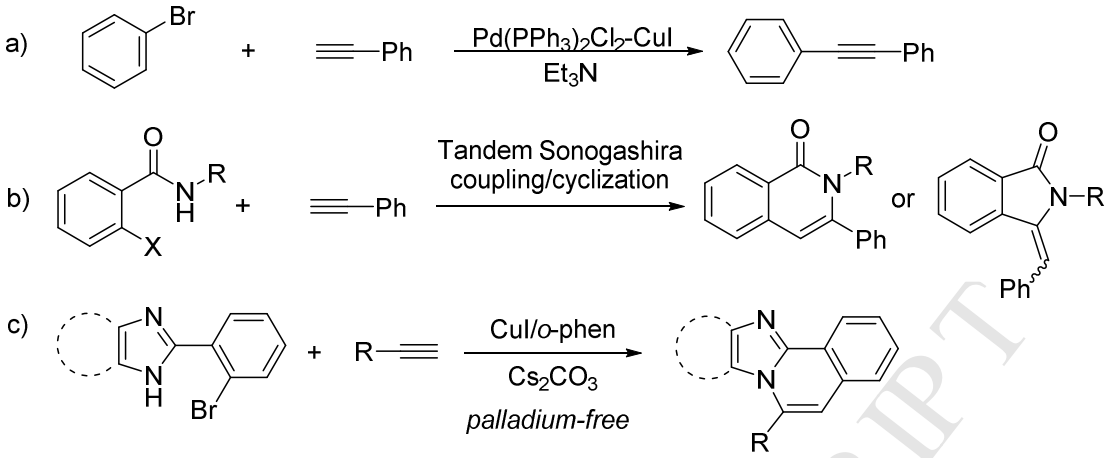
Abstract: The Sonogashira reaction first, and then intra-molecular hydroamination of alkyne catalyzed by CuI/*o*-phen was proved to be an efficient method for the synthesis of imidazo[2,1-*a*] isoquinoline, phenanthro[9',10':4,5]imidazo[2,1-*a*]isoquinoline and acenaphtho[1',2':4,5]imidazo [2,1-*a*]isoquinoline derivatives in the presence of Cs_2CO_3.

Keywords: Sonogashira reaction, hydroamination, imidazoisoquinoline, CuI/*o*-phen

1. Introduction

Sonogashira reaction is such a well-known cross-coupling for the formation of C(sp)-C(sp^2) bond that terminal alkyne with aryl halide or vinyl halide conventionally perform with the treatment of Pd-Cu co-catalyst and a base, such as well-established $Pd(PPh_3)_2Cl_2$-CuI-Et_3N system (Scheme 1, path a).[1] In recent years, 2-halogenated benzamides have been applied to the Sonogashira reaction which in turn underwent an alkyne hydroamination to deliver the resulting isoquinoline or isoindole derivatives (Scheme 1, path b).[2-4] In 2016, Chen et al. reported the CuI-catalysed tandem Sonogashira coupling/6-*endo* cyclization protocol for the assembly of fused triazolo[5,1-*a*]isoquinolines in good to excellent yields.[5] Of which, the triazole moiety on 4-(2-bromophenyl)-2*H*-1,2,3-triazole was utilized as a *N*-base nucleophilic component for alkyne hydroamination. Hence, the merge Sonogashira reaction into a tandem manner provided an efficient access for the synthesis of fused polycyclic heterocycles. For instance, imidazoisoquinolines possess good pharmacological and biological activities, such as antimalarial, anti-thrombotic, antisecretory and antitumor activities.[6-9]

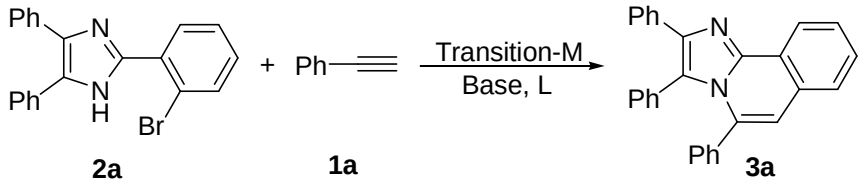


Scheme 1. Sonogashira approaches for the synthesis of alkynes and *N*-containing heterocycles

A range of imidazo[2,1-*a*]isoquinoline derivatives, including 2-(2-bromophenyl)-4,5-diphenyl-1*H*-imidazole (**2**), 2-(2-bromophenyl)-1*H*-phenanthro[9,10-*d*]imidazole (**4**) and 8-(2-bromophenyl)-7*H*-acenaphtho[1,2-*d*] imidazole (**6**) were synthesized first in our lab, and then they were submitted to react with phenylacetylenes, respectively. It is reasonable that the imino group on 1*H*-imidazole attacks the alkynyl functions delivering a new C–N single bond after the Sonogashira reaction. To our delight, the resulting annulation products imidazo[2,1-*a*]isoquinolines were obtained in good yields, respectively. As our continious study on the construction of polycyclic heterocycles catalyzed by copper,[10] herein, we present the tandem Sonogashira approach for the generation of imidazo[2,1-*a*]isoquinolines with the corresponding *N*-heteroaryl bromides and terminal alkynes which undergoes in the presenc of CuI/*o*-phen as catalyt and Cs_2CO_3 as the base (Scheme 1, path c).

2. Results and discussion

The hypothesis was first examined using phenylacetylene (**1a**) and 2-(2-bromophenyl)-4,5-diphenyl-1*H*-imidazole (**2a**) as the model substrate to screen the reaction conditions involving different transition-metal catalysts, ligands and bases (Scheme 2).



Scheme 2. The model reaction catalyzed by transition-metals

Initially, the model reaction of **1a** and **2a** was conducted under the available Sonogashira reaction using 5 mol% $Pd(PPh_3)_2Cl_2$ and 10 mol% CuI as co-catalyst, Et_3N as a base in refluxing THF, leading to the corresponding product **3a** in high yields (89%) (Table 1, entry 1). When reducing the ammount of palladium catalyst to 1 mol%, the yield is silightly lower to 79%. While in the absence of $Pd(PPh_3)_2Cl_2$ **3a** was still obtained in 32% yield (Table 1, entry 2). Thus, a further exploration of palladium-free conditions was conducted. First, in the presence of CuI (10mol%) as the catalyst, several ligands such as PPh_3, *L*-proline, *o*-phenanthroline (*o*-phen) and $MeNHCH_2CO_2H$ (Figure 1) were evaluated and displayed that *o*-phen resulted in the best results with 79% yield of **3a** (Table 1, entry 5). When using copper(I) salts e.g., CuBr and CuCl as the catalyst with *o*-phen, the reaction still underwent smoothly but furnished slightly lower yields (Table 1, entries 7 and 8). Whereas, copper(II) salts such $CuBr_2$ and $CuCl_2$ were unreactive to promote the desired reaction (Table 1, entries 9 and 10). Other organic base (e.g., DBU), or inorganic bases including K_2CO_3, Cs_2CO_3, and $NaHCO_3$ were also tested with the combination of CuI and *o*-phen, and Cs_2CO_3 (100 mol%) provided the best result (82%, Table 1, entry 13). Screening numerous solvents such as such as DME, toluene, DMF and DMSO showed that dioxane performed better, generating the desired product in 88% yield at 100 °C (88%, Table 1, entry 16). After attempting various conditions, we obtained the expected result by using CuI (10 mol%), *o*-phen (20 mol%), Cs_2CO_3 (1.0 equiv.), in dioxane at

100 °C. In contrast, an attempt with the previous conditions[5] in the presence of CuI and K_2CO_3 at 110 °C in DMSO was conducted, however, affording **3a** in 46% yield.

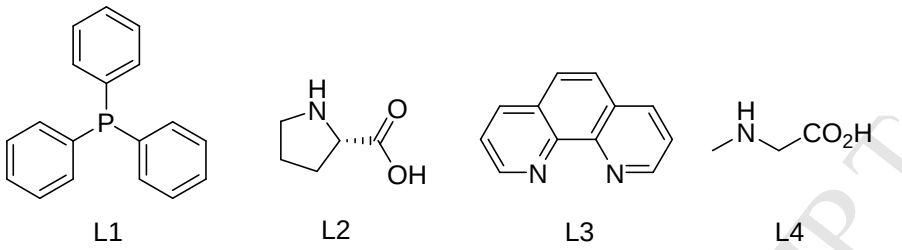
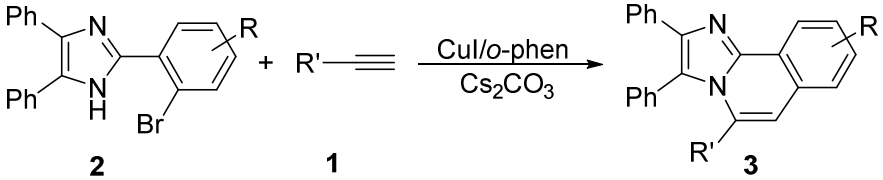


Figure 1. The structures of ligands

Table 1. Optimization of Reaction Conditions for **1a** and **2a**[a]

Entry	Cat./mol%	L/mol%	Base	solvent	T/°C	Yields/%[b]
1	Pd-Cu[c]	_	Et_3N	THF	Reflux	89
2	CuI(10)	_	Et_3N	THF	Reflux	32
3	CuI(10)	L1(20)	Et_3N	THF	Reflux	52
4	CuI(10)	L2(20)	Et_3N	THF	Reflux	65
5	CuI(10)	L3(20)	Et_3N	THF	Reflux	79
6	CuI(10)	L4(20)	Et_3N	THF	Reflux	62
7	CuBr(10)	L3(20)	Et_3N	THF	Reflux	72
8	CuCl(10)	L3(20)	Et_3N	THF	Reflux	65
9	$CuBr_2$(10)	L3(20)	Et_3N	THF	Reflux	-
10	$CuCl_2$(10)	L3(20)	Et_3N	THF	Reflux	-
11	CuI(10)	L3(20)	DBU	THF	Reflux	73
12	CuI(10)	L3(20)	K_2CO_3	THF	Reflux	75
13	CuI(10)	L3(20)	Cs_2CO_3	THF	Reflux	82
14	CuI(10)	L3(20)	$NaHCO_3$[d]	THF	Reflux	65
15	CuI(10)	L3(20)	Cs_2CO_3	DME	Reflux	79
16	CuI(10)	L3(20)	Cs_2CO_3	Dioxane	Reflux	88
17	CuI(10)	L3(20)	Cs_2CO_3	Toluene	Reflux	64
18	CuI(10)	L3(20)	Cs_2CO_3	DMF	100	75
19	CuI(10)	L3(20)	Cs_2CO_3	DMSO	100	78

[a] Reaction condition: **1a** (374 mg, 1.0 mmol), **2a** (122 mg, 1.2 mmol), base (1.0 mmol), solvent (10.0 mL); [b] isolated yields; [c] $Pd(PPh_3)_2Cl_2$ (5 mol%) and CuI (10 mol%); [d] 2.0 mmol.



2 **1** **3**

Scheme 3. The Sonogashira reaction and cyclization of **1** and **2**

Table 2. The reaction time and yields of the products **3**

Entry	R	R'	Products	Time/h	Yields/%
1	H	C_6H_5	**3a**	24	88
2	8-Cl	C_6H_5	**3b**	22	79
3	9-Cl	C_6H_5	**3c**	20	80
4	9-F	C_6H_5	**3d**	26	86
5	9-MeO	C_6H_5	**3e**	22	78
6	8,9-OCH_2O	C_6H_5	**3f**	26	82
7	9-F	4-EtC_6H_4	**3g**	26	81
8	8-Me	4-EtC_6H_4	**3h**	24	84
9	9-MeO	4-EtC_6H_4	**3i**	26	68
10	8,9-OCH_2O	4-EtC_6H_4	**3j**	22	78
11	9-Cl	4-$MeOC_6H_4$	**3k**	24	80
12	9-Cl	Cyclopropyl	**3l**	26	78
13	8,9-$(MeO)_2$	Cyclopropyl	**3m**	24	82

Reaction condition: **1** (1.0 mmol), **2** (1.0 mmol), CuI (20 mg, 0.1 mmol), *o*-phen (36 mg, 0.2 mmol), Cs_2CO_3 (325 mg, 1.0 mmol), dioxane (10.0 mL), 100 °C.

With the optimized conditions, we examined the scope of this tandem protocol by using functionalized phenylacetylene with 2-(2-bromophenyl)-4,5-diphenyl-1*H*-imidazole (Scheme 3). The results are summarized in Table 2. Both electron-donating groups (e.g., Me, Et, MeO) and electron-withdrawing groups (e.g., F and Cl) in the benzene moieties were applicable and delivered the desired imidazo[2,1-*a*] isoquinoline derivatives **3a-3k** in good yield. To our delight, cyclopropyl acetylene were also tolerant under the same reaction conditions and afforded the resulting 3-cyclopropylimidazo[2,1-*a*]isoquinolines (**3l-3m**) in 78% and 82% yields, respectively. The molecular structure of **3d** was further confirmed by X-ray diffraction analysis, and its crystal structure was shown in Figure 2.

X-ray diffraction analysis of **3d** reveals that all the ring including the central pyridine are coplanar. The imidazole moiety is nearly parallel to the isoquinoline ring, forming a dihedral angle of 6.8 (1)°. The dihedral angles between the imidazole and two benzene rings (C12-C17, and C18-C23) are 37.2 (1) and 60.2 (1)°, respectively.

Another benzene ring (C24-C29) makes a dihedral angle of 54.5 (1)° to the isoquinoline moiety.

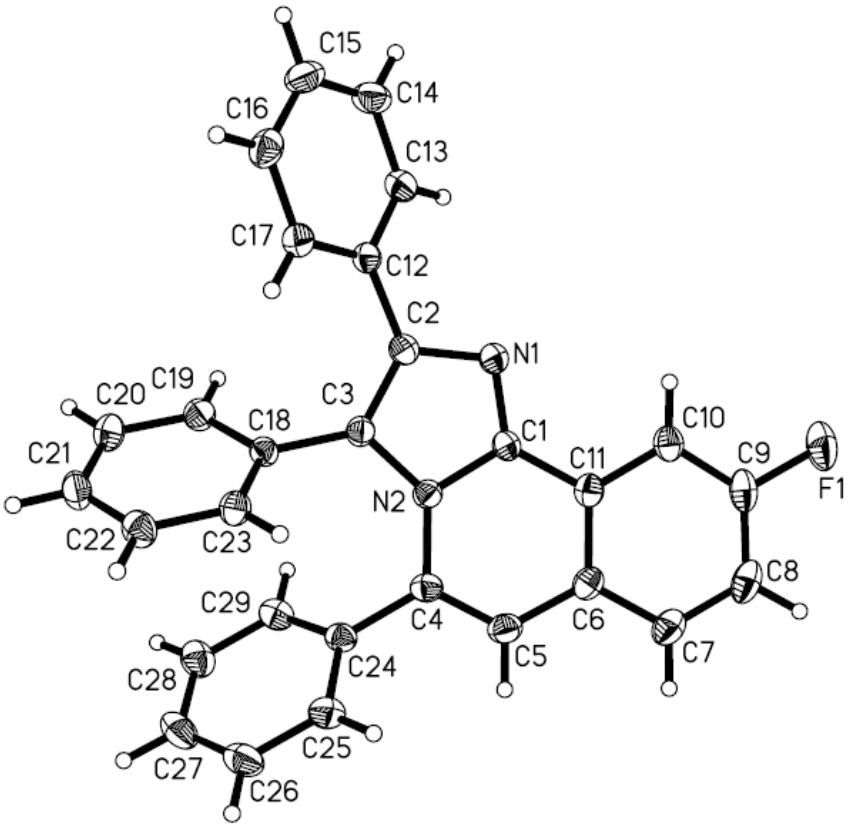
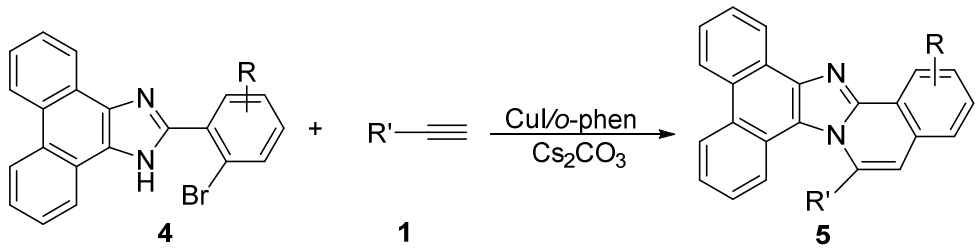


Figure 2. The crystal structure of **3d**

A range of modified 2-(2-bromophenyl) imidazole substrates, 2-(2-bromo phenyl)-1*H*-phenanthro[9,10-*d*]imidazoles (**4**) were synthesized by a three-component reaction of 9,10-phenanthrenequinone, ammonium acetate and 2-bromobenzaldehyde. Sequently, the materials (**4**) were submitted to react with phenylacetylene under the same reaction conditions (Scheme 4). To our great delight, all of the 2-(2-bromophenyl)-1*H*-phenanthro[9,10-*d*]imidazoles were applicable and afforded the corresponding **5a**-**5l** in good yields (Table 3). Both aryl- and cyclopropyl substituted alkynes were well efficient under the reaction conditions.



4 1 5

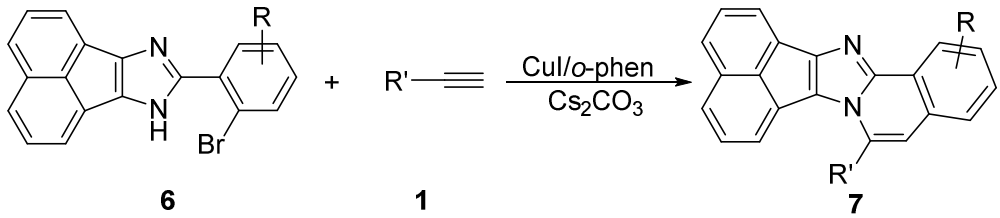
Scheme 4. The Sonogashira reaction and cyclization of **1** and **4**

Table 3. The reaction time and yields of the products **5**

Entry	R	R’	Products	Time/h	Yields/%
1	H	C_6H_5	**5a**	20	80
2	3-Cl	C_6H_5	**5b**	22	89
3	2-Cl	C_6H_5	**5c**	22	88
4	2-MeO	C_6H_5	**5d**	24	86
5	3-Cl	4-MeC_6H_4	**5e**	26	78
6	2-Cl	4-MeC_6H_4	**5f**	22	88
7	2-Cl	4-EtC_6H_4	**5g**	24	85
8	2-MeO	4-EtC_6H_4	**5h**	26	88
9	2-MeO	4-$EtOC_6H_4$	**5i**	24	84
10	2-MeO	4-(*n*-Pr)C_6H_4	**5j**	24	85
11	3-Cl	Cyclopropyl	**5k**	26	91
12	2-Cl	Cyclopropyl	**5l**	26	82

Reaction condition: **1** (1.0 mmol), **4** (1.0 mmol), CuI (20 mg, 0.1 mmol), *o*-phen (36 mg, 0.2 mmol), Cs_2CO_3 (325 mg, 1.0 mmol), dioxane (10.0 mL), 100 °C.

Analogously, 2-(2-bromophenyl)imidazole compounds, 8-(2-bromophenyl)-7*H*-acenaphtho[1,2-*d*] imidazole (**6**) were also treated with phenylacetylene under similar conditions (Scheme 5), albeit all reactions required slightly longer time to complete the intermolecular coupling and subsequent intramolecular cyclization. As a result, the 8-(2-bromophenyl)-7*H*-acenaphtho[1,2-*d*]imidazole substrates proved to be reactive and led to the corresponding 13-arylacenaphtho[1',2':4,5]imidazo[2,1-*a*] isoquinoline derivatives **7a-g** in moderate to good yields (Table 4).



6 1 7

Scheme 5. The Sonogashira reaction and cyclization of **1** and **6**

Table 4. The reaction time and yields of the products **7**

Entry	R	R'	Products	Time/h	Yields/%
1	H	Ph	**7a**	28	76
2	H	4-EtC_6H_4	**7b**	26	78
3	H	4-(*n*-Pr)C_6H_4	**7c**	30	80
4	9-F	Cyclopropyl	**7d**	26	68
5	9-F	4-EtC_6H_4	**7e**	29	79
6	9-F	4-(*n*-Pr)C_6H_4	**7f**	30	82
7	9-Cl	Cyclopropyl	**7g**	32	80

Reaction condition: **1** (1.0 mmol), **6** (1.0 mmol), CuI (20 mg, 0.1 mmol), *o*-phen (36 mg, 0.2 mmol), Cs_2CO_3 (325 mg, 1.0 mmol), dioxane (10.0 mL), 100 °C.

3. Conclusion

In summary, we have developed a CuI/*o*-phen catalysed tandem Sonogashira coupling/hydroamination approach of 2-(2-bromophenyl)imidazoles and terminal alkynes affording a variety of imidazo[2,1-*a*]isoquinoline-based fused polycyclic compounds in good yields. A range of 2-(2-bromophenyl)imidazole derivatives with highly polycyclic aromatics were applicable under the optimal conditions.

4. Experimental

Melting points were determined in open capillaries and are uncorrected. IR spectra were recorded on a TENSOR 27 spectrometer in KBr. NMR spectra were obtained from solution in $CDCl_3$ with Me_4Si as internal standard using a BRUKER-400 spectrometer. HRMS analyses were carried out using a Bruker-micro-TOF-Q-MS analyzer.

4.1. General procedure for the preparation of the substates 2, 4 and 6 (Using 2a as a model)[11,12]

Benzil (4.204 g, 20 mmol), 2-bromobenzaldehyde (3.700 g, 20 mmol) and NH_4OAc (6.160 g, 80 mmol) were added to a mixture of ethyl alcohol (50.0 mL) and glacial acetic acid (5.0 mL). The mixture was refluxing until all the benzil was consumed which was monitoried by TLC. After the completion of the reaction, the

desired **2a** was obtained as the yellow crystals by a filtration when the mixture was allowed to cool down to room temperarure, 92% yield, m.p. 202-203 °C (Lit.[11] 201-202 °C). The **4** and **6** were prepared by the same procedure using phenanthrene-9,10-dione and acenaphthylene-1,2-dione as the *o*-diketones, respectively.

4.2. General procedure for the syntheses of imidazo[2,1-*a*]isoquinoline 3

A dry 50 mL flask was charged with phenylacetylene **1** (1.0 mmol), 2-(2-bromoaryl)-4,5-diphenyl-1*H*-imidazole **2** (1.0 mmol), CuI (20 mg, 0.1 mmol), *o*-phen (36 mg, 0.2 mmol), Cs_2CO_3 (325 mg, 1.0 mmol), dioxane (10.0 mL). The reaction mixture was stirred at 100 °C for 20-26 h under N_2 atmosphere until all the **2** was consumed. The insoluble substance was romoved by a fast hot filtration, and the filtrate was concentrated under reduced pressure. The residue was purified by a column chromatography to give **3** using a mixture of ethyl acetate and petroleum ether (1 : 8) as an eluant.

2,3,5-Triphenylimidazo[2,1-*a*]isoquinoline (**3a**): M.p. 212~214 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 6.90~7.10 (m, 11H, ArH), 7.17~7.25 (m, 3H, ArH), 7.50~7.52 (m, 2H, ArH), 7.57~7.61 (m, 1H, ArH), 7.65~7.71 (m, 2H, ArH), 8.88 (d, *J* = 8.0 Hz, 1H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 115.7, 123.3, 123.7, 124.5, 126.5, 126.9, 127.3, 127.4, 127.77, 127.82, 128.0, 128.3, 128.5, 129.2, 129.3, 131.4, 134.4, 134.7, 137.0, 141.7, 143.8. IR (KBr): ν 3056, 1716, 1684, 1653, 1635, 1559, 1540, 1507, 1489, 1473, 1418, 1396, 1379, 1339, 1025, 915, 846, 777, 763 cm^{-1}. HRMS (ESI, *m/z*): Calcd for $C_{29}H_{21}N_2$ $[M + H]^+$ 397.1704, found 397.1708.

8-Chloro-2,3,5-triphenylimidazo[2,1-*a*]isoquinoline (**3b**): M.p. 208~210 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 6.83 (s, 1H, ArH), 6.89~7.10 (m, 10H, ArH), 7.17~7.25 (m, 3H, ArH), 7.47~7.50 (m, 2H, ArH), 7.60 (dd, *J* = 8.8 Hz, *J*' = 2.0 Hz, 1H, ArH), 7.67

(d, J = 2.0 Hz, 1H, ArH), 8.80 (d, J = 8.8 Hz, 1H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 114.5, 121.6, 124.7, 125.4, 125.6, 127.1, 127.44, 127.47, 127.8, 128.1, 128.3, 128.5, 129.1, 130.4, 131.2, 131.4, 133.97, 134.04, 134.5, 138.3, 142.0, 143.3. IR (KBr): ν 3057, 1632, 1598, 1526, 1498, 1472, 1446, 1422, 1379, 1336, 1323, 1235, 1197, 1158, 1116, 1081, 1027, 942, 915, 887, 820, 763, 753, 701 cm^{-1}. HRMS (ESI, *m/z*): Calcd for $C_{29}H_{20}ClN_2$ $[M + H]^+$ 431.1315, found 431.1318.

9-Chloro-2,3,5-triphenylimidazo[2,1-*a*]isoquinoline (**3c**): M.p. 193~195 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 6.88~7.00 (m, 7H, ArH), 7.02~7.10 (m, 4H, ArH), 7.17~7.25 (m, 3H, ArH), 7.48~7.53 (m, 3H, ArH), 7.63 (d, J = 8.8 Hz, 1H, ArH), 8.87 (d, J = 2.4 Hz, 1H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 115.0, 123.1, 124.3, 124.9, 127.1, 127.45, 127.52, 127.8, 128.0, 128.1, 128.2, 128.4, 128.7, 129.1, 131.1, 131.3, 133.7, 134.1, 134.4, 137.3, 142.0, 142.8. IR (KBr): ν 3031, 2964, 1540, 1507, 1490, 1473, 1442, 1419, 1375, 1302, 1095, 1020, 917, 879, 868, 858, 815, 764, 749, 709 cm^{-1}. HRMS (ESI, *m/z*): Calcd for $C_{29}H_{20}ClN_2$ $[M + H]^+$ 431.1315, found 431.1315.

9-Fluoro-2,3,5-triphenylimidazo[2,1-*a*]isoquinoline (**3d**): M.p. 192~193 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 6.90~7.10 (m, 11H, ArH), 7.17~7.25 (m, 3H, ArH), 7.29~7.34 (m, 1H, ArH), 7.48~7.51 (m, 2H, ArH), 7.69 (dd, J = 8.8 Hz, J' = 5.2 Hz, 1H, ArH), 8.51 (dd, J = 9.6 Hz, J' = 2.8 Hz, 1H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 108.9 (d, $J_{(F-C)}$ = 23.0 Hz), 115.0, 117.1 (d, $J_{(F-C)}$ = 24.0 Hz), 124.8, 124.9, 125.9 (d, $J_{(F-C)}$ = 1.8 Hz), 127.1, 127.5, 127.8, 128.07, 128.11, 128.5, 128.8 (d, $J_{(F-C)}$ = 8.0 Hz), 129.2, 131.2, 131.4, 134.2, 134.5, 136.3 (d, $J_{(F-C)}$ = 2.7 Hz), 141.9, 143.1 (d, $J_{(F-C)}$ = 4.7 Hz), 162.1 (d, $J_{(F-C)}$ = 246.0 Hz). IR (KBr): ν 3056, 3005, 2960, 2836, 1599, 1508, 1473, 1441, 1375, 1303, 1247, 1174, 1108, 1073, 1031, 918, 862, 834, 811, 775, 750, 702 cm^{-1}. HRMS (ESI, *m/z*): Calcd for $C_{29}H_{20}FN_2$ $[M + H]^+$ 415.1610, found 415.1604.

9-Methoxy-2,3,5-triphenylimidazo[2,1-*a*]isoquinoline (**3e**): M.p. 198~200 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 4.08 (m, 3H, OCH_3), 6.90~7.09 (m, 11H, ArH), 7.18~7.24 (m, 4H, ArH), 7.50~7.52 (m, 2H, ArH), 7.62 (d, *J* = 8.4 Hz, 1H, ArH), 8.32 (d, *J* = 2.0 Hz, 1H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 56.1, 103.7, 115.8, 119.5, 123.7, 124.4, 124.6, 127.1, 127.3, 127.4, 127.7, 127.9, 128.1, 128.2, 128.6, 129.2, 131.2, 131.4, 134.5, 134.6, 134.7, 141.6, 143.6, 159.5. IR (KBr): ν 3055, 2967, 1601, 1523, 1495, 1436, 1380, 1355, 1245, 1217, 1193, 1103, 1027, 912, 860, 816, 773, 757 cm^{-1}. HRMS (ESI, *m/z*): Calcd for $C_{30}H_{23}N_2O$ $[M + H]^+$ 427.1810, found 427.1807.

2,3,5-Triphenyl-[1,3]dioxolo[4,5-*g*]imidazo[2,1-*a*]isoquinoline (**3f**): M.p. 230~231 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 6.13 (s, 2H, CH_2), 6.79 (s, 1H, ArH), 6.89~7.08 (m, 11H, ArH), 7.16~7.24 (m, 3H, ArH), 7.48~7.51 (m, 2H, ArH), 8.24 (s, 1H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 101.5, 102.2, 104.3, 115.4, 119.2, 123.8, 125.6, 126.9, 127.2, 127.4, 127.7, 127.9, 128.0, 128.5, 128.6, 129.0, 129.2, 131.4, 131.5, 134.4, 134.8, 135.5, 141.5, 144.0, 148.5, 149.0. IR (KBr): ν 3053, 2909, 1521, 1501, 1476, 1442, 1382, 1311, 1249, 1196, 1141, 1118, 1040, 944, 911, 886, 863, 833, 773, 756, 722 cm^{-1}. HRMS (ESI, *m/z*): Calcd for $C_{30}H_{21}N_2O_2$ $[M + H]^+$ 441.1603, found 441.1603.

5-(4-Ethylphenyl)-9-fluoro-2,3-diphenylimidazo[2,1-*a*]isoquinoline (**3g**): M.p. 211~213 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 1.17 (t, *J* = 7.6 Hz, 3H, CH_3), 2.51 (q, *J* = 7.6 Hz, 2H, CH_2), 6.79 (d, *J* = 7.6 Hz, 2H, ArH), 6.88~6.97 (m, 7H, ArH), 7.02~7.05 (m, 1H, ArH), 7.19~7.25 (m, 3H, ArH), 7.28~7.33 (m, 1H, ArH), 7.49~7.51 (m, 2H, ArH), 7.68 (dd, *J* = 8.8 Hz, *J*' = 5.2 Hz, 1H, ArH), 8.50 (dd, *J* = 9.6 Hz, *J*' = 2.4 Hz, 1H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 15.7, 28.7, 108.9 (d, $J_{(F-C)}$ = 23.6 Hz), 114.6, 117.1 (d, $J_{(F-C)}$ = 23.9 Hz), 124.7 (d, $J_{(F-C)}$ = 9.8 Hz), 124.9, 126.0 (d, $J_{(F-C)}$ = 1.9 Hz),126.9, 127.0, 127.3, 127.7, 128.1, 128.5, 128.7 (d, $J_{(F-C)}$ = 8.7 Hz), 129.2,

131.3, 131.4, 131.5, 134.6, 136.5 (d, $J_{(F-C)}$ = 2.8 Hz), 141.8, 143.1 (d, $J_{(F-C)}$ = 4.6 Hz), 144.3, 162.0 (d, $J_{(F-C)}$ = 245.9 Hz). IR (KBr): ν 3058, 2965, 1601, 1532, 1508, 1483, 1444, 1377, 1309, 1233, 1189, 1142, 1098, 1020, 916, 833, 805, 774, 700 cm^{-1}. HRMS (ESI, *m/z*): Calcd for $C_{31}H_{24}FN_2$ $[M + H]^+$ 443.1923, found 443.1920.

5-(4-Ethylphenyl)-9-methyl-2,3-diphenylimidazo[2,1-*a*]isoquinoline (**3h**): M.p. 166~168 °C; ^1H NMR ($CDCl_3$, 400 MHz): δ_H 1.17 (t, *J* = 7.6 Hz, 3H, CH_3), 2.51 (q, *J* = 7.6 Hz, 2H, CH_2), 2.54 (s, 3H, CH_3), 6.78 (d, *J* = 8.0 Hz, 2H, ArH), 6.84 (s, 1H, ArH), 6.88~7.03 (m, 7H, ArH), 7.15~7.24 (m, 3H, ArH), 7.47~7.51 (m, 4H, ArH), 8.75 (d, *J* = 8.8 Hz, 1H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 15.7, 21.8, 28.7, 115.2, 121.1, 123.7, 124.3, 126.1, 126.8, 126.9, 127.1, 127.6, 128.0, 128.5, 129.2, 129.4, 129.6, 131.5, 131.6, 131.8, 134.9, 137.2, 138.2, 141.4, 144.0, 144.2. IR (KBr): ν 3025, 2958, 1559, 1540, 1507, 1473, 1457, 1375, 1327, 911, 894, 836, 773, 747, 717, 701 cm^{-1}. HRMS (ESI, *m/z*): Calcd for $C_{32}H_{27}N_2$ $[M + H]^+$ 439.2174, found 439.2175.

5-(4-Ethylphenyl)-9-methoxy-2,3-diphenylimidazo[2,1-*a*]isoquinoline (**3i**): M.p. 175~176 °C; ^1H NMR ($CDCl_3$, 400 MHz): δ_H 1.17 (t, *J* = 7.6 Hz, 3H, CH_3), 2.51 (q, *J* = 7.6 Hz, 2H, CH_2), 4.07 (s, 3H, OCH_3), 6.78 (d, *J* = 8.0 Hz, 2H, ArH), 6.87~6.97 (m, 7H, ArH), 7.00~7.02 (m, 1H, ArH), 7.16~7.25 (m, 4H, ArH), 7.50~7.52 (m, 2H, ArH), 7.61 (d, *J* = 8.8 Hz, 1H, ArH), 8.25 (d, *J* = 2.4 Hz, 1H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 15.8, 28.7, 55.9, 103.7, 115.1, 119.2, 123.7, 124.5, 124.6, 126.9, 127.1, 127.6, 128.0, 128.1, 128.6, 129.3, 131.4, 131.5, 131.8, 134.8, 134.9, 141.6, 143.6, 144.0, 159.4. IR (KBr): ν 3026, 2965, 1559, 1541, 1508, 1490, 1473, 1465, 1457, 1438, 1250, 1218, 1153, 1103, 1023, 867, 837, 776, 702 cm^{-1}. HRMS (ESI, *m/z*): Calcd for $C_{32}H_{27}N_2O$ $[M + H]^+$ 455.2123, found 455.2120.

5-(4-Ethylphenyl)-2,3-diphenyl-[1,3]dioxolo[4,5-*g*]imidazo[2,1-*a*]isoquinoline (**3j**): M.p. 188~190 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 1.16 (t, J = 7.6 Hz, 3H, CH_3), 2.50 (q, J = 7.6 Hz, 2H, CH_2), 6.11 (s, 2H, CH_2), 6.77 (d, J = 8.0 Hz, 3H, ArH), 6.87~6.95 (m, 6H, ArH), 6.99~7.03 (m, 2H, ArH), 7.15~7.24 (m, 3H, ArH), 7.49~7.51 (m, 2H, ArH), 8.23 (s, 1H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 15.8, 28.7, 101.5, 102.1, 104.3, 115.0, 119.1, 123.8, 125.6, 126.8, 126.9, 127.0, 127.6, 128.0, 128.5, 128.6, 129.0, 129.2, 131.4, 131.6, 131.7, 134.8, 135.7, 141.4, 144.0, 144.1, 148.4, 148.9. IR (KBr): ν 3051, 2958, 1507, 1470, 1448, 1379, 1316, 1244, 1196, 1144, 1116, 1034, 950, 910, 965, 881, 869, 833, 789, 773, 700 cm^{-1}. HRMS (ESI, *m/z*): Calcd for $C_{32}H_{25}N_2O_2$ $[M + H]^+$ 469.1916, found 469.1915.

9-Chloro-5-(4-methoxyphenyl)-2,3-diphenylimidazo[2,1-*a*]isoquinoline (**3k**): M.p. 220~222 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 3.73 (s, 3H, OCH_3), 6.49 (d, J = 8.8 Hz, 2H, ArH), 6.86~6.91 (m, 3H, ArH), 6.96~7.00 (m, 4H, ArH), 7.06~7.10 (m, 1H, ArH), 7.19~7.24 (m, 3H, ArH), 7.48~7.53 (m, 3H, ArH), 7.62 (d, J = 8.4 Hz, 1H, ArH), 8.86 (d, J = 1.6 Hz, 1H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 55.3, 112.9, 114.5, 123.1, 124.2, 124.9, 126.5, 127.0, 127.2, 127.6, 127.75, 127.83, 128.0, 128.5, 128.7, 130.4, 131.3, 131.4, 133.4, 134.5, 137.1, 142.0, 142.7, 159.4. IR (KBr): ν 3052, 1602, 1541, 1494, 1473, 1445, 1376, 1340, 1307, 1235, 1190, 1144, 1117, 1100, 1073, 1027, 886, 864, 818, 778, 760, 706 cm^{-1}. HRMS (ESI, *m/z*): Calcd for $C_{30}H_{22}ClN_2O$ $[M + H]^+$ 461.1420, found 461.1416.

9-Chloro-5-cyclopropyl-2,3-diphenylimidazo[2,1-*a*]isoquinoline (**3l**): M.p. 173~174 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 0.36~0.41 (m, 2H, CH_2), 0.62~0.66 (m, 2H, CH_2), 1.54~1.61 (m, 1H, CH), 6.70 (s, 1H, ArH), 7.17~7.26 (m, 3H, ArH), 7.39~7.47 (m, 4H, ArH), 7.51~7.56 (m, 5H, ArH), 8.77 (d, J = 2.0 Hz, 1H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 8.7, 15.9, 110.1, 123.0, 124.1, 124.7, 127.0, 127.5, 127.7,

127.9, 128.0, 128.1, 128.5, 128.7, 132.6, 133.0, 133.1, 134.5, 139.3, 141.7, 142.3. IR (KBr): ν 3015, 1598, 1531, 1473, 1442, 1396, 1300, 1173, 1101, 1075, 1025, 883, 860, 842, 776, 758, 718 cm^{-1}. HRMS (ESI, *m/z*): Calcd for $C_{26}H_{20}ClN_2$ $[M + H]^+$ 395.1315, found 395.1314.

5-Cyclopropyl-8,9-dimethoxy-2,3-diphenylimidazo[2,1-*a*]isoquinoline (**3m**): M.p. 264~266 °C; ^1H NMR ($CDCl_3$, 400 MHz): δ_H 0.33~0.38 (m, 2H, CH_2), 0.60~0.64 (m, 2H, CH_2), 1.55~1.62 (m, 1H, CH), 4.00 (s, 3H, OCH_3), 4.13 (m, 3H, OCH_3), 6.69 (s, 1H, ArH), 6.99 (s, 1H, ArH), 7.15~7.25 (m, 3H, ArH), 7.37~7.45 (m, 3H, ArH), 7.54~7.58 (m, 4H, ArH), 8.17 (s, 1H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 8.6, 15.9, 56.0, 56.5, 104.2, 106.4, 110.5, 117.3, 123.8, 124.4, 126.8, 127.8, 128.0, 218.47, 128.54, 132.7, 133.4, 137.3, 141.1, 143.3, 149.8, 150.5. IR (KBr): ν 3054, 2994, 2956, 2832, 1640, 1600, 1533, 1495, 1439, 1394, 1309, 1247, 1225, 1163, 1123, 1103, 1027, 1006, 919, 863, 782, 757, 706 cm^{-1}. HRMS (ESI, *m/z*): Calcd for $C_{28}H_{25}N_2O_2$ $[M + H]^+$ 421.1916, found 421.1917.

4.3. General procedure for the syntheses of phenanthro[9',10':4,5] imidazo[2,1-*a*]isoquinolines 5

A dry 50 mL flask was charged with phenylacetylene **1** (1.0 mmol), 2-(2-bromophenyl)-1*H*-phenanthro[9,10-*d*]imidazole **4** (1.0 mmol), CuI (20 mg, 0.1 mmol), *o*-phen (36 mg, 0.2 mmol), Cs_2CO_3 (325 mg, 1.0 mmol), dioxane (10.0 mL). The reaction mixture was stirred at 100 °C for 20-26 h under N_2 atmosphere until all the **4** was consumed. The aftertreatment and purification of products **5** (The volume ratio of ethyl acetate and petroleum ether is 1 : 6) were same to those of **3**.

6-Phenylphenanthro[9',10':4,5]imidazo[2,1-*a*]isoquinoline (**5a**): M.p. 231~232 °C; ^1H NMR ($CDCl_3$, 400 MHz): δ_H 6.92~6.96 (m, 1H, ArH), 7.02 (dd, J = 8.4 Hz, J' = 0.8 Hz, 1H, ArH), 7.28 (s, 1H, ArH), 7.32~7.42 (m, 4H, ArH), 7.48~7.50 (m, 2H, ArH),

7.67~7.85 (m, 5H, ArH), 8.67~8.71 (m, 2H, ArH), 9.03~9.06 (m, 2H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 116.3, 123.0, 123.1, 123.3, 123.6, 124.0, 124.5, 124.65, 124.67, 126.56, 126.60, 126.7, 127.2, 128.1, 128.3, 129.0, 129.1, 129.3, 129.7, 130.6, 137.0, 137.8, 140.6, 148.1. IR (KBr): ν 3051, 1577, 1559, 1518, 1470, 1456, 1416, 1380, 1337, 1304, 1278, 1237, 1146, 1128, 1025, 950, 876, 842, 778, 770, 750, 725 cm^{-1}. HRMS (ESI, *m/z*): Calcd for $C_{29}H_{19}N_2$ $[M + H]^+$ 395.1548, found 395.1557.

3-Chloro-6-phenylphenanthro[9',10':4,5]imidazo[2,1-*a*]isoquinoline (**5b**): M.p. 269~270 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 6.90~6.95 (m, 2H, ArH), 7.12 (s, 1H, ArH), 7.30~7.44 (m, 6H, ArH), 7.64 (dd, *J* = 8.4 Hz, *J'* = 1.6 Hz, 1H, ArH), 7.69~7.72 (m, 1H, ArH), 7.76~7.80 (m, 2H, ArH), 8.65~8.69 (m, 2H, ArH), 8.92 (d, *J* = 8.8 Hz, 1H, ArH), 8.99 (dd, *J* = 8.0 Hz, *J'* = 0.4 Hz, 1H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 115.0, 121.6, 122.96, 123.01, 123.4, 123.6, 124.2, 124.6, 124.7, 125.9, 126.3, 126.6, 126.7, 127.1, 127.3, 128.4, 128.5, 129.1, 129.4, 129.8, 131.6, 135.1, 136.6, 139.0, 140.7, 147.5. IR (KBr): ν 3052, 1559, 1540, 1507, 1458, 1447, 1412, 1377, 1321, 1277, 1255, 1197, 1152, 1077, 1039, 938, 869, 834, 773, 752, 722, 708 cm^{-1}. HRMS (ESI, *m/z*): Calcd for $C_{29}H_{18}ClN_2$ $[M + H]^+$ 429.1158, found 429.1158.

2-Chloro-6-phenylphenanthro[9',10':4,5]imidazo[2,1-*a*]isoquinoline (**5c**): M.p. 266~268 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 6.91~6.98 (m, 2H, ArH), 7.22 (s, 1H, ArH), 7.31~7.39 (m, 4H, ArH), 7.40~7.47 (m, 2H, ArH), 7.61 (dd, *J* = 8.4 Hz, *J'* = 2.0 Hz, 1H, ArH), 7.69~7.81 (m, 3H, ArH), 8.66~8.70 (m, 2H, ArH), 9.00~9.02 (m, 2H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 115.5, 123.0, 123.1, 123.4, 123.6, 124.1, 124.2, 124.3, 124.6, 124.8, 126.6, 126.8, 127.1, 127.4, 128.2, 128.5, 128.8, 129.1, 129.3, 129.7, 129.8, 133.9, 136.7, 138.0, 140.7, 146.9. IR (KBr): ν 3058, 1653, 1636, 1559, 1540, 1507, 1490, 1472, 1457, 1448, 1410, 1386, 1277, 1072, 1021, 874, 865,

807, 772 cm^{-1}. HRMS (ESI, *m/z*): Calcd for $C_{29}H_{18}ClN_2$ $[M + H]^+$ 429.1158, found 429.1158.

2-Methoxy-6-phenylphenanthro[9',10':4,5]imidazo[2,1-*a*]isoquinoline (**5d**): M.p. 245~247 °C; ^1H NMR ($CDCl_3$, 400 MHz): δ_H 4.13 (s, 3H, OCH_3), 6.91~6.95 (m, 1H, ArH), 7.03 (d, *J* = 8.0 Hz, 1H, ArH), 7.23 (s, 1H, ArH), 7.27~7.38 (m, 5H, ArH), 7.44~7.46 (m, 2H, ArH), 7.68~7.81 (m, 3H, ArH), 8.41 (d, *J* = 2.4 Hz, 1H, ArH), 8.66~8.71 (m, 2H, ArH), 9.05 (dd, *J* = 8.0 Hz, *J'* = 1.2 Hz, 1H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 55.9, 104.7, 116.3, 120.2, 122.97, 123.00, 123.2, 123.3, 123.6, 123.9, 124.5, 124.6, 124.7, 124.8, 126.47, 126.52, 127.2, 127.3, 128.3, 128.4, 128.8, 129.0, 129.7, 135.5, 137.2, 140.5, 147.9, 159.6. IR (KBr): ν 3064, 1612, 1559, 1533, 1507, 1497, 1447, 1436, 1413, 1355, 1280, 1196, 1092, 1030, 867, 848, 814, 771, 763, 751, 725 cm^{-1}. HRMS (ESI, *m/z*): Calcd for $C_{30}H_{21}N_2O$ $[M + H]^+$ 425.1654, found 425.1660.

3-Chloro-6-(*p*-tolyl)phenanthro[9',10':4,5]imidazo[2,1-*a*]isoquinoline (**5e**): M.p. 247~248 °C; ^1H NMR ($CDCl_3$, 400 MHz): δ_H 2.39 (s, 3H, CH_3), 6.93~6.97 (m, 1H, ArH), 7.02 (d, *J* = 8.0 Hz, 1H, ArH), 7.13~7.16 (m, 3H, ArH), 7.34~7.40 (m, 3H, ArH), 7.65 (dd, *J* = 8.4 Hz, *J'* = 2.0 Hz, 1H, ArH), 7.69~7.73 (m, 1H, ArH), 7.77~7.80 (m, 2H, ArH), 8.67~8.71 (m, 2H, ArH), 8.94 (d, *J* = 8.4 Hz, 1H, ArH), 9.00 (d, *J* = 8.0 Hz, 1H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 21.4, 114.6, 121.5, 123.0, 123.06, 123.08, 123.4, 123.6, 124.1, 124.5, 125.0, 125.8, 126.2, 126.5, 126.7, 127.1, 127.3, 128.3, 128.4, 129.7, 129.8, 131.7, 133.8, 135.1, 139.2, 139.6, 140.7, 147.5. IR (KBr): ν 3031, 1559, 1540, 1521, 1490, 1465, 1414, 1374, 1323, 1278, 1238, 1182, 1078, 894, 881, 817, 751, 726 cm^{-1}. HRMS (ESI, *m/z*): Calcd for $C_{30}H_{20}ClN_2$ $[M + H]^+$ 443.1315, found 443.1315.

2-Chloro-6-(*p*-tolyl)phenanthro[9',10':4,5]imidazo[2,1-*a*]isoquinoline (**5f**): M.p. 199~201 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 2.39 (m, 3H, CH_3), 6.93~6.97 (m, 1H, ArH), 7.03 (d, *J* = 7.2 Hz, 1H, ArH), 7.14 (d, *J* = 8.4 Hz, 2H, ArH), 7.19 (s, 1H, ArH), 7.34~7.40 (m, 3H, ArH), 7. 7.61 (dd, *J* = 8.4 Hz, *J*' = 2.0 Hz, 1H, ArH), 7.70~7.75 (m, 2H, ArH), 7.78~7.81 (m, 1H, ArH), 8.67~8.70 (m, 2H, ArH), 8.99~9.02 (m, 2H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 21.4, 115.0, 122.96, 123.04, 123.2, 123.4, 123.6, 124.0, 124.17, 124.20, 124.5, 125.1, 126.5, 126.7, 127.1, 127.3, 128.1, 128.5, 128.9, 129.6, 129.7, 129.8, 133.7, 133.9, 138.2, 139.5, 140.7, 146.9. IR (KBr): ν 3027, 1595, 1533, 1511, 1467, 1449, 1413, 1381, 1337, 1307, 1277, 1235, 1188, 1111, 1071, 1020, 952, 875, 864, 822, 771, 748, 727, 707 cm^{-1}. HRMS (ESI, *m/z*): Calcd for $C_{30}H_{20}ClN_2$ $[M + H]^+$ 443.1315, found 443.1318.

2-Chloro-6-(4-ethylphenyl)phenanthro[9',10':4,5]imidazo[2,1-*a*]isoquinoline (**5g**): M.p. 270~272 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 1.24 (t, *J* = 7.6 Hz, 3H, CH_3), 2.67 (q, *J* = 7.6 Hz, 2H, CH_2), 6.88~6.96 (m, 2H, ArH), 7.14~7.17 (m, 3H, ArH), 7.34~7.38 (m, 3H, ArH), 7.59 (dd, *J* = 8.4 Hz, *J*' = 2.0 Hz, 1H, ArH), 7.68~7.72 (m, 2H, ArH), 7.76~7.80 (m, 1H, ArH), 8.65~8.68 (m, 2H, ArH), 8.97~9.01 (m, 2H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 15.9, 28.8, 114.9, 122.92, 123.02, 123.2, 123.3, 123.6, 124.0, 124.1, 124.2, 124.5, 125.1, 126.7, 127.1, 127.3, 128.0, 128. 44, 128.52, 128.8, 129.6, 129.8, 133.6, 134.1, 138.2, 140.6, 146.0, 146.9. IR (KBr): ν 3063, 2962, 2927, 2872, 1540, 1508, 1466, 1418, 1411, 1380, 1338, 1320, 1277, 1072, 968, 864, 832, 804, 754, 725, 700 cm^{-1}. HRMS (ESI, *m/z*): Calcd for $C_{31}H_{22}ClN_2$ $[M + H]^+$ 457.1471, found 457.1468.

6-(4-Ethylphenyl)-2-methoxyphenanthro[9',10':4,5]imidazo[2,1-*a*]isoquinoline (**5h**): M.p. 244~245 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 1.25 (t, *J* = 7.6 Hz, 3H, CH_3), 2.67 (q, *J* = 7.6 Hz, 2H, CH_2), 4.13 (s, 3H, OCH_3), 6.91~6.94 (m, 1H, ArH), 7.04 (d, *J* =

8.0 Hz, 1H, ArH), 7.15 (d, *J* = 8.0 Hz, 2H, ArH), 7.23 (s, 1H, ArH), 7.29 (dd, *J* = 8.8 Hz, *J*' = 2.8 Hz, 1H, ArH), 7.35~7.38 (m, 3H, ArH), 7.69~7.81 (m, 3H, ArH), 8.42 (d, *J* = 2.8 Hz, 1H, ArH), 8.67~8.72 (m, 2H, ArH), 9.05~9.07 (m, 1H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 16.0, 28.8, 55.9, 104.7, 115.8, 120.1, 123.0, 123.1, 123.3, 123.6, 123.9, 124.46, 124.51, 125.0, 126.5, 126.6, 127.2, 127.3, 128.28, 128.32, 128.5, 129.7, 134.6, 135.7, 140.4, 145.5, 147.9, 159.5. IR (KBr): ν 3013, 2956, 2867, 1609, 1533, 1508, 1488, 1437, 1381, 1355, 1254, 1196, 1186, 1145, 1030, 868, 848, 836, 811, 754, 724, 705 cm^{-1}. HRMS (ESI, *m/z*): Calcd for $C_{32}H_{25}N_2O$ $[M + H]^+$ 453.1967, found 453.1957.

6-(4-Ethoxyphenyl)-2-methoxyphenanthro[9',10':4,5]imidazo[2,1-*a*]isoquinoline (**5i**): M.p. 249~250 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 1.41 (t, *J* = 7.2 Hz, 3H, CH_3), 4.03 (q, *J* = 7.6 Hz, 2H, CH_2), 4.13 (s, 3H, OCH_3), 6.83 (d, *J* = 8.4 Hz, 2H, ArH), 6.99~7.03 (m, 1H, ArH), 7.14 (d, *J* = 8.4 Hz, 1H, ArH), 7.18 (s, 1H, ArH), 7.29 (dd, *J* = 8.8 Hz, *J*' = 2.8 Hz, 1H, ArH), 7.37~7.40 (m, 3H, ArH), 7.69~7.74 (m, 2H, ArH), 7.77~7.81 (m, 1H, ArH), 8.41 (d, *J* = 2.4 Hz, 1H, ArH), 8.67~8.71 (m, 2H, ArH), 9.05 (d, *J* = 8.0 Hz, 1H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 16.0, 28.8, 55.9, 100.0, 104.6, 115.8, 120.2, 123.0, 123.1, 123.3, 123.6, 123.9, 124.46, 124.47, 125.0, 126.5, 126.6, 127.2, 127.3, 128.26, 128.32, 128.5, 129.7, 134.5, 135.7, 140.4, 145.4, 147.9, 159.5. IR (KBr): ν 3033, 2981, 1541, 1508, 1489, 1473, 1418, 1283, 1248, 1230, 1178, 1092, 1039, 923, 964, 835, 752, 727 cm^{-1}. HRMS (ESI, *m/z*): Calcd for $C_{32}H_{25}N_2O_2$ $[M + H]^+$ 469.1916, found 469.1917.

2-Methoxy-6-(4-*n*-propylphenyl)phenanthro[9',10':4,5]imidazo[2,1-*a*]isoquinoline (**5j**): M.p. 231~232 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 0.96 (t, *J* = 8.0 Hz, 3H, CH_3), 1.60~1.69 (m, 2H, CH_2), 2.60 (t, *J* = 7.2 Hz, 2H, CH_2), 4.12 (s, 3H, OCH_3), 6.90~6.94 (m, 1H, ArH), 7.05 (d, *J* = 8.0 Hz, 1H, ArH), 7.12 (d, *J* = 8.0 Hz, 2H, ArH), 7.21 (s,

1H, ArH), 7.29 (dd, *J* = 8.8 Hz, *J*' = 2.8 Hz, 1H, ArH), 7.33~7.37 (m, 3H, ArH), 7.68~7.74 (m, 2H, ArH), 7.77~7.80 (m, 1H, ArH), 8.41 (d, *J* = 2.8 Hz, 1H, ArH), 8.66~8.71 (m, 2H, ArH), 9.04~9.06 (m, 1H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 13.7, 24.6, 37.8, 55.9, 104.6, 115.8, 120.1, 123.0, 123.1, 123.3, 123.5, 123.8, 124.45, 124.47, 124.9, 125.0, 126.4, 126.5, 127.2, 127.3, 128.2, 128.3, 129.1, 129.7, 134.6, 135.7, 140.4, 143.7, 147.9, 159.5. IR (KBr): ν 3058, 2959, 2870, 2827, 1614, 1533, 1511, 1488, 1436, 1417, 1382, 1354, 1280, 1232, 1200, 1146, 1092, 1032, 867, 846, 819, 770, 750, 725 cm^{-1}. HRMS (ESI, *m/z*): Calcd for $C_{33}H_{27}N_2O$ $[M + H]^+$ 467.2123, found 467.2133.

3-Chloro-6-cyclopropylphenanthro[9',10':4,5]imidazo[2,1-*a*]isoquinoline (**5k**): M.p. 216~217 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 1.01~1.05 (m, 2H, CH_2), 1.25~1.30 (m, 2H, CH_2), 2.55~2.61 (m, 1H, CH), 6.66 (s, 1H, ArH), 7.54~7.61 (m, 3H, ArH), 7.64 (d, *J* = 1.6 Hz, 1H, ArH), 7.70~7.73 (m, 1H, ArH), 7.76~7.79 (m, 1H, ArH), 8.58~8.60 (m, 1H, ArH), 8.72 (d, *J* = 8.4 Hz, 1H, ArH), 8.76~8.78 (m, 1H, ArH), 8.82 (d, *J* = 8.4 Hz, 1H, ArH), 8.95 (d, *J* = 8.0 Hz, 1H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 12.3, 16.3, 107.4, 121.1, 122.9, 123.0, 123.5, 124.16, 124.20, 124.5, 124.9, 125.0, 125.2, 126.1, 126.7 127.1, 127.4, 127.5, 128.6, 129.7, 131.9, 134.9, 141.2, 142.6, 147.5. IR (KBr): ν 3043, 1539, 1463, 1448, 1414, 1324, 1257, 1238, 1172, 1161, 1102, 1072, 1041, 1023, 980, 946, 921, 869, 824, 809, 724, 711 cm^{-1}. HRMS (ESI, *m/z*): Calcd for $C_{26}H_{18}ClN_2$ $[M + H]^+$ 393.1158, found 393.1151.

2-Chloro-6-cyclopropylphenanthro[9',10':4,5]imidazo[2,1-*a*]isoquinoline (**5l**): M.p. 229~230 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 1.00~1.04 (m, 2H, CH_2), 1.23~1.28 (m, 2H, CH_2), 2.54~2.61 (m, 1H, CH), 6.72 (s, 1H, ArH), 7.53 (dd, *J* = 8.8 Hz, *J*' = 2.0 Hz, 1H, ArH), 7.56~7.61 (m, 3H, ArH), 7.69~7.73 (m, 1H, ArH), 7.77~7.79 (m, 1H, ArH), 8.57~7.61 (m, 1H, ArH), 8.71 (d, *J* = 8.0 Hz, 1H, ArH), 8.74~8.78 (m, 1H, ArH), 8.87

(d, *J* = 1.6 Hz, 1H, ArH), 8.94 (d, *J* = 8.0 Hz, 1H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 12.2, 16.3, 107.9, 122.96, 123.04, 123.5, 123.8, 123.9, 124.16, 124.19, 124.6, 125.0, 125.1, 126.7, 127.1, 127.2, 127.4, 128.6, 129.0, 129.5, 129.7, 132.8, 141.1, 141.5, 146.9. IR (KBr): ν 3074, 3006, 1636, 1596, 1571, 1544, 1532, 1471, 1448, 1404, 1323, 1259, 1237, 1175, 1108, 1068, 1041, 986, 949, 901, 883, 846, 821, 773, 754, 727 cm^{-1}. HRMS (ESI, *m/z*): Calcd for $C_{26}H_{18}ClN_2$ $[M + H]^+$ 393.1158, found 393.1155.

4.4. General procedure for the syntheses of acenaphtho[1',2':4,5] imidazo[2,1-*a*]isoquinolines 7

A dry 50 mL flask was charged with phenylacetylene **1** (1.0 mmol), 8-(2-bromoaryl)-7*H*-acenaphtho[1,2-*d*]imidazole **6** (1.0 mmol), CuI (20 mg, 0.1 mmol), *o*-phen (36 mg, 0.2 mmol), Cs_2CO_3 (325 mg, 1.0 mmol), dioxane (10.0 mL). The reaction mixture was stirred at 100 °C for 26-32 h under N_2 atmosphere until all the **6** was consumed. The aftertreatment and purification of products **7** (The volume ratio of ethyl acetate and petroleum ether is 1 : 5) were the same as those of **3**.

13-Phenylacenaphtho[1',2':4,5]imidazo[2,1-*a*]isoquinoline (**7a**): M.p. 290~292 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 5.05 (d, *J* = 6.8 Hz, 1H, ArH), 7.05~7.08 (m, 2H, ArH), 7.54~7.75 (m, 11H, ArH), 8.10 (d, *J* = 7.2 Hz, 1H, ArH), 8.81 (d, *J* = 8.0 Hz, 1H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 114.5, 121.1, 121.2, 123.6, 123.8, 125.9, 126.9, 127.2, 127.3, 127.5, 127.8, 128.1, 128.2, 129.18, 129.21, 129.5, 129.8, 130.0, 130.6, 131.9, 135.57, 135.64, 148.3, 151.5. IR (KBr): ν 3044, 1528, 1492, 1474, 1438, 1282, 1224, 1180, 1123, 1040, 903, 870, 816, 781, 765, 749 cm^{-1}. HRMS (ESI, *m/z*): Calcd for $C_{27}H_{17}N_2$ $[M + H]^+$ 369.1391, found 369.1390.

13-(4-Ethylphenyl)acenaphtho[1',2':4,5]imidazo[2,1-*a*]isoquinoline (**7b**): M.p. 218~220 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 1.42 (t, *J* = 7.6 Hz, 3H, CH_3), 2.88 (q, *J*

= 7.6 Hz, 2H, CH_2), 5.03 (d, *J* = 7.2 Hz, 1H, ArH), 7.02~7.06 (m, 2H, ArH), 7.46 (d, *J* = 7.6 Hz, 2H, ArH), 7.53~7.60 (m, 5H, ArH), 7.64~7.74 (m, 3H, ArH), 8.09 (d, *J* = 6.8 Hz, 1H, ArH), 8.80 (d, *J* = 8.0 Hz, 1H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 16.3, 29.1, 114.2, 121.2, 123.6, 123.7, 125.9, 126.8, 127.05, 127.10, 127.3, 127.4, 127.8, 128.0, 128.1, 128.2, 128.7, 129.2, 129.6, 130.0, 130.1, 131.9, 133.0, 134.5, 135.7, 146.5, 151.4. IR (KBr): ν 3036, 2954, 2925, 1529, 1509, 1473, 1461, 1438, 1410, 1388, 1280, 1220, 1187, 1121, 1042, 1021, 971, 932, 870, 842, 832, 818, 768, 748, 801 cm^{-1}. HRMS (ESI, *m/z*): Calcd for $C_{29}H_{21}N_2$ $[M + H]^+$ 397.1704, found 397.1700.

13-(4-Propylphenyl)acenaphtho[1',2':4,5]imidazo[2,1-*a*]isoquinoline (**7**c): M.p. 223~225 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 1.11 (t, *J* = 7.2 Hz, 3H, CH_3), 1.79~1.88 (m, 2H, CH_2), 2.81 (t, *J* = 7.6 Hz, 2H, CH_2), 5.07 (d, *J* = 7.2 Hz, 1H, ArH), 7.01~7.06 (m, 2H, ArH), 7.43 (d, *J* = 7.6 Hz, 2H, ArH), 7.53~7.60 (m, 5H, ArH), 7.64~7.73 (m, 3H, ArH), 8.09 (d, *J* = 6.8 Hz, 1H, ArH), 8.80 (d, *J* = 8.0 Hz, 1H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 13.8, 24.9, 38.0, 114.3, 121.2, 123.6, 123.7, 125.9, 126.8, 127.1, 127.3, 127.4, 127.8, 128.0, 128.1, 129.2, 129.3, 129.6, 129.9, 130.0, 130.6, 131.9, 133.0, 135.7, 144.7, 148.3, 151.4. IR (KBr): ν 3036, 2957, 2925, 2857, 1556, 1508, 1473, 1437, 1410, 1284, 1226, 1186, 1122, 1038, 1022, 947, 932, 909, 844, 818, 768, 746, 721, 701 cm^{-1}. HRMS (ESI, *m/z*): Calcd for $C_{30}H_{23}N_2$ $[M + H]^+$ 411.1861, found 411.1862.

13-Cyclopropyl-9-fluoroacenaphtho[1',2':4,5]imidazo[2,1-*a*]isoquinoline (**7d**): M. p.252~255 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 1.04~1.08 (m, 2H, CH_2), 1.25~1.30 (m, 2H, CH_2), 2.58~2.65 (m, 1H, CH), 6.75 (s, 1H, ArH), 7.17~7.22 (m, 1H, ArH), 7.43~7.46 (m, 1H, ArH), 7.53~7.62 (m, 2H, ArH), 7.67 (d, *J* = 8.4 Hz, 1H, ArH), 7.73 (d, *J* = 7.2 Hz, 1H, ArH), 7.76 (d, *J* = 8.0 Hz, 1H, ArH), 8.08 (d, *J* = 7.2 Hz, 1H, ArH),

8.29 (d, J = 7.6 Hz, 1H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 8.2, 14.7, 108.5 (d, $J_{(F-C)}$ = 23.7 Hz), 109.5, 116.8 (d, $J_{(F-C)}$ = 24.0 Hz), 120.8, 121.2, 124.7 (d, $J_{(F-C)}$ = 9.8 Hz), 126.0 (d, $J_{(F-C)}$ = 1.7 Hz), 126.3, 127.3, 127.5, 127.7, 128.0, 128.5, 128.6, 129.6, 129.8, 130.5, 132.2, 136.6 (d, $J_{(F-C)}$ = 2.7 Hz), 147.6 (d, $J_{(F-C)}$ = 5.4 Hz), 151.7, 160.3 (d, $J_{(F-C)}$ = 245.6 Hz). IR (KBr): ν 3041, 2925, 2855, 1534, 1488, 1459, 1280, 1268, 1224, 1200, 1182, 1157, 1123, 1075, 1038, 997, 955, 933, 896, 862, 817, 798, 763, 747 cm^{-1}. HRMS (ESI, *m/z*): Calcd for $C_{24}H_{16}FN_2$ $[M + H]^+$ 351.1297, found 351.1290.

13-(4-Ethylphenyl)-9-fluoroacenaphtho[1',2':4,5]imidazo[2,1-*a*]isoquinoline (**7e**): M.p. 269~271 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 1.42 (t, J = 7.6 Hz, 3H, CH_3), 2.87 (q, J = 7.6 Hz, 2H, CH_2), 5.04 (d, J = 7.2 Hz, 1H, ArH), 7.03~7.07 (m, 2H, ArH), 7.28~7.33 (m, 1H, ArH), 7.46 (d, J = 7.6 Hz, 2H, ArH), 7.55~7.58 (m, 4H, ArH), 7.69~7.73 (m, 2H, ArH), 8.09 (d, J = 6.8 Hz, 1H, ArH), 8.42 (dd, J = 9.6 Hz, J' = 2.4 Hz, 1H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 15.6, 28.7, 107.7 (d, $J_{(F-C)}$ = 22.1 Hz), 117.5, 121.6 (d, $J_{(F-C)}$ = 25.6 Hz), 122.7, 125.7 (d, $J_{(F-C)}$ = 8.7 Hz), 127.1, 127.2, 128.3, 129.0, 130.3 (d, $J_{(F-C)}$ = 8.6 Hz), 131.8, 131.9, 134.7, 136.08, 136.14, 145.0, 148.3, 148.4, 150.9 (d, $J_{(F-C)}$ = 2.7 Hz), 161.5 (d, $J_{(F-C)}$ = 248.8 Hz), 164.3. IR (KBr): ν 2963, 2926, 2854, 1508, 1483, 1460, 1377, 1350, 1301, 1274, 1262, 1231, 1189, 1154, 1097, 1039, 952, 931, 899, 872, 849, 819, 769, 720 cm^{-1}. HRMS (ESI, *m/z*): Calcd for $C_{29}H_{20}FN_2$ $[M + H]^+$ 415.1610, found 415.1614.

9-Fluoro-13-(4-*n*-propylphenyl)acenaphtho[1',2':4,5]imidazo[2,1-*a*]isoquinoline (**7f**): M.p. 270~272 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 1.11 (t, J = 7.2 Hz, 3H, CH_3), 1.79~1.88 (m, 2H, CH_2), 2.81 (t, J = 7.6 Hz, 2H, CH_2), 5.06 (d, J = 7.2 Hz, 1H, ArH), 7.01~7.05 (m, 2H, ArH), 7.27~7.31 (m, 1H, ArH), 7.43 (d, J = 8.0 Hz, 2H, ArH), 7.54~7.58 (m, 4H, ArH), 7.67~7.72 (m, 2H, ArH), 8.08 (d, J = 6.8 Hz, 1H, ArH), 8.42

(dd, J = 9.6 Hz, J' = 2.4 Hz, 1H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 13.8, 24.9, 38.0, 108.6 (d, $J_{(F-C)}$ = 23.7 Hz), 113.6, 117.0 (d, $J_{(F-C)}$ = 23.9 Hz), 121.2, 121.4, 125.1 (d, $J_{(F-C)}$ = 9.7 Hz), 126.0, 126.1 (d, $J_{(F-C)}$ = 2.0 Hz), 127.1, 127.4, 127.5, 127.6, 129.1, 129.19, 129.23, 129.3, 129.8, 129.9, 132.0, 132.8, 135.0 (d, $J_{(F-C)}$ = 2.7 Hz), 144.8, 147.5 (d, $J_{(F-C)}$ = 4.7 Hz), 151.5, 162.1 (d, $J_{(F-C)}$ = 246.4 Hz). IR (KBr): ν 3039, 2964, 2927, 2867, 1525, 1508, 1460, 1435, 1350, 1299, 1265, 1224, 1144, 1130, 1096, 1067, 1049, 1010, 965, 921, 882, 851, 832, 816, 767, 742, 719 cm^{-1}. HRMS (ESI, *m/z*): Calcd for $C_{30}H_{22}FN_2$ $[M + H]^+$ 429.1767, found 429.1759.

9-Chloro-13-cyclopropylacenaphtho[1',2':4,5]imidazo[2,1-*a*]isoquinoline (**7g**): M.p. 272~274 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 1.08~1.12 (m, 2H, CH_2), 1.29~1.34 (m, 2H, CH_2), 2.64~2.71 (m, 1H, CH), 6.78 (s, 1H, ArH), 7.41~7.53 (m, 3H, ArH), 7.60~7.64 (m, 1H, ArH), 7.71 (d, J = 8.0 Hz, 1H, ArH), 7.76~7.80 (m, 2H, ArH), 8.09 (d, J = 6.8 Hz, 1H, ArH), 8.67 (s, 1H, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 8.2, 14.8, 109.4, 120.9, 121.3, 122.9, 124.3, 126.5, 127.4, 127.6, 127.69, 127.73, 127.8, 128.0, 128.4, 129.7, 129.8, 130.6, 132.2, 133.4, 137.6, 147.3, 151.8. IR (KBr): ν 3040, 2955, 2928, 2868, 1606, 1559, 1508, 1473, 1437, 11411, 1375, 1300, 1274, 1224, 1187, 1154, 1121, 1041, 952, 906, 819, 769 cm^{-1}. HRMS (ESI, *m/z*): Calcd for $C_{24}H_{16}ClN_2$ $[M + H]^+$ 367.1002, found 367.1000.

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