JOC The Journal of Organic Chemistry

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$Cu(OAc)_2$-Catalyzed Aerobic Oxidative Dehydrogenation Coupling: Synthesis of Heptacyclic Quinolizino[3,4,5,6-*kla*]perimidines

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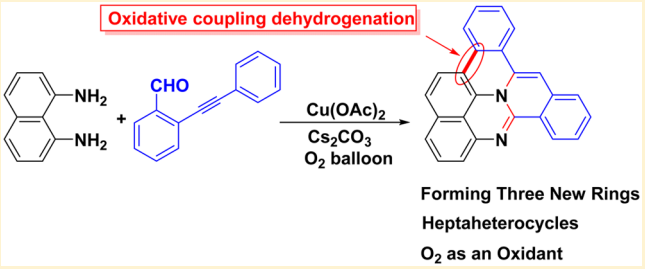
Supporting Information

ABSTRACT: A $Cu(OAc)_2$-catalyzed domino tricyclization between naphthalene-1,8-diamine and 2-(phenylethynyl)-benzaldehyde is described, enabling aerobic oxidative dehydrogenation coupling to access heptacyclic quinolizino[3,4,5,6-*kla*]perimidines. In this reaction, the formation of three new rings and four new bonds was achieved in a functional-group-compatible fashion, allowing a facile method toward fused aza-heterocycles containing both quinolizine and perimidine moieties.



Oxidative dehydrogenation coupling of aromatic $C(sp^2)-H$ bonds is a highly efficient approach for the synthesis of biaryls.[1] Learning from the previous reports, valuable metals have been largely employed, for example, Pd,[2] Mo,[3] Rh,[4] and Ru.[5] In the presence of various oxidizing agents, such as Ag^+,[6] $S_2O_8^{2-}$,[7] or TBHP,[8] especially for air or oxygen,[9] only one molecule of water is lost from the reactants; therefore, it has good atom economy concerning green chemistry. In the past few years, oxidative dehydrogenation has been used in organic synthesis to construct structurally diverse biphenyls or polycyclic heterocycles.[10,11] Heptacyclic quinolizino[3,4,5,6-*kla*]perimidine is a highly conjugated heterocycle in which the derivatives are widely applied in electronic materials, such as in dye lasers and electroluminescent materials.[12] In 2011, Fujii and co-workers[13] reported the two-step procedure for the generation of heptacyclic quinolizino[3,4,5,6-*kla*]perimidines through a copper-catalyzed bicyclization between *o*-(2-bromophenyl)ethynyl-substituted arylaldehydes with 1,8-diaminonaphthalene and a palladium-catalyzed C−H arylation in sequence (Scheme 1a). However, a backbone bromo-functional group was required for the C−H arylation process.

Enlightened by this reaction, we reasoned that under suitable catalytic oxidation conditions tricyclization of 2-alkynylbenzaldehydes and 1,8-diaminonaphthalene could be achieved in a one-pot operation through aerobic oxidative coupling and dehydrogenation, enabling $C(sp^2)-C(sp^2)$ bond formation to access highly conjugated heptacyclic quinolizino[3,4,5,6-*kla*]-perimidines under Pd- and halogen-free conditions. Based on the above analysis, we selected $Cu(OAc)_2$ as a catalyst to conduct this reaction considering its low cost and high catalytic activity.[14] As part of our continuing interest in the design of copper-catalyzed domino reaction for significant aza-heterocycle synthesis,[15] herein we report this copper-catalyzed domino tricyclization for the synthesis of heptacyclic quinolizino[3,4,5,6-*kla*]perimidines via a sequential cyclization, alkyne hydroamination, and oxidative dehydrogenation coupling (Scheme 1b).

We began our optimization studies with 1,8-diaminonaphthalene (**1**) and 2-(phenylethynyl)benzaldehyde (**2a**) as model substrates by verifying the catalysts, oxidants, bases, solvent, and temperature (Table 1). Initially, this reaction was carried out in the presence of $Cu(OAc)_2$ (1.2 equiv) at 130 °C in DMSO under an argon atmosphere.[14] However, only a trace product of **3a** was observed by TLC. Different oxidants, such as $PhI(OAc)_2$, $K_2S_2O_8$, Ag_2O, DDQ, and air, were employed, and the expected product **3a** was obtained in 8% yield under air conditions, whereas other oxidants completely suppressed the reaction process (entries 2−5). Furthermore, various bases including K_2CO_3, Cs_2CO_3, Na_2CO_3, and $NaHCO_3$ were evaluated (entries 7−10). Among the bases tested, the use of Cs_2CO_3 (100 mol %) gave in the best result with a 16% yield (entry 8), whereas isoquinolino[2,1-*a*]perimidine intermediate **4a** was isolated in 66% yield. Decreasing the loading of $Cu(OAc)_2$ to 20 mol % also furnished **3a** with a 16% yield under air conditions (entry 12). A further decrease the dosage of $Cu(OAc)_2$ was adverse to the yield of **3a** (entry 13). To our delight, the yield of **3a** was improved to 62% dramatically under an oxygen atmosphere in the presence of 1.0 equiv of Cs_2CO_3 in DMSO (entry 14). Afterward, the solvent effect was investigated. THF, 1,4-dioxane, and toluene were tested, and 1,4-dioxane was proved to be the best medium for this tricyclization, delivering **3a** in a 76% yield (entry 14). Compared to $Cu(OAc)_2$, other copper(II) salts ($CuCl_2$ and $Cu(OTf)_2$) were completely ineffective for this transformation. Moreover, the copper(I) species CuI was also reactive, affording the desired product **3a** in 71% yield (entry 20).

Received: November 2, 2016
Published: December 28, 2016

DOI: 10.1021/acs.joc.6b02644
J. Org. Chem. 2017, 82, 1817−1822

Scheme 1. Synthesis of Heptacyclic Quinolizino[3,4,5,6-*kla*]perimidines

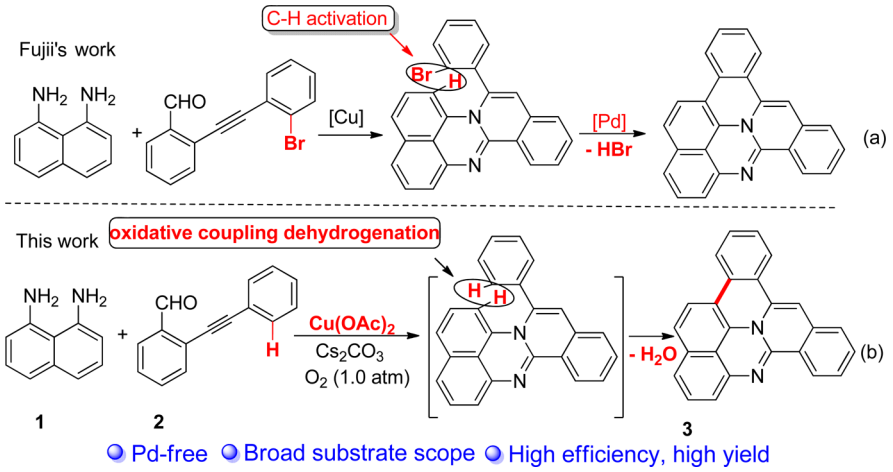
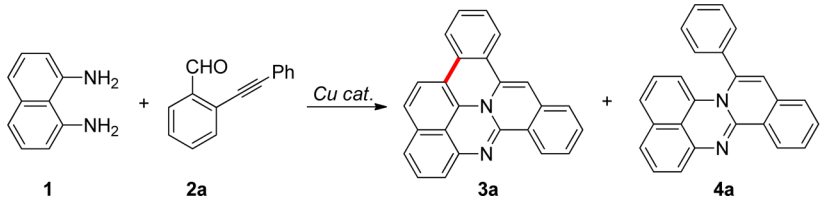


Table 1. Optimization Studies for Copper-Mediated Oxidative Coupling and Dehydrogenation[a]



entry	cat. (mol %)	oxidant (mol %)	base[b]	solvent	yield of **3a**[c] (%)
1	$Cu(OAc)_2$(120)			DMSO	trace
2	$Cu(OAc)_2$(120)	$PhI(OAc)_2$(100)		DMSO	trace
3	$Cu(OAc)_2$(120)	$K_2S_2O_8$(100)		DMSO	trace
4	$Cu(OAc)_2$(120)	Ag_2O(100)		DMSO	trace
5	$Cu(OAc)_2$(120)	DDQ(100)		DMSO	trace
6	$Cu(OAc)_2$(120)	air		DMSO	8
7	$Cu(OAc)_2$(120)	air	K_2CO_3	DMSO	12
8	$Cu(OAc)_2$(120)	air	Cs_2CO_3	DMSO	16
9	$Cu(OAc)_2$(120)	air	Na_2CO_3	DMSO	10
10	$Cu(OAc)_2$(120)	air	$NaHCO_3$	DMSO	10
11	$Cu(OAc)_2$(50)	air	Cs_2CO_3	DMSO	15
12	$Cu(OAc)_2$(20)	air	Cs_2CO_3	DMSO	16
13	$Cu(OAc)_2$(10)	air	Cs_2CO_3	DMSO	12
14[d]	$Cu(OAc)_2$(20)	O_2	Cs_2CO_3	DMSO	62
15	$Cu(OAc)_2$(20)	O_2	Cs_2CO_3	dioxane	76
16[e]	$Cu(OAc)_2$(20)	O_2	Cs_2CO_3	THF	21
17	$Cu(OAc)_2$(20)	O_2	Cs_2CO_3	toluene	69
18	$CuCl_2$(20)	O_2	Cs_2CO_3	dioxane	trace
19	$Cu(OTf)_2$(20)	O_2	Cs_2CO_3	dioxane	trace
20	CuI(20)	O_2	Cs_2CO_3	dioxane	70

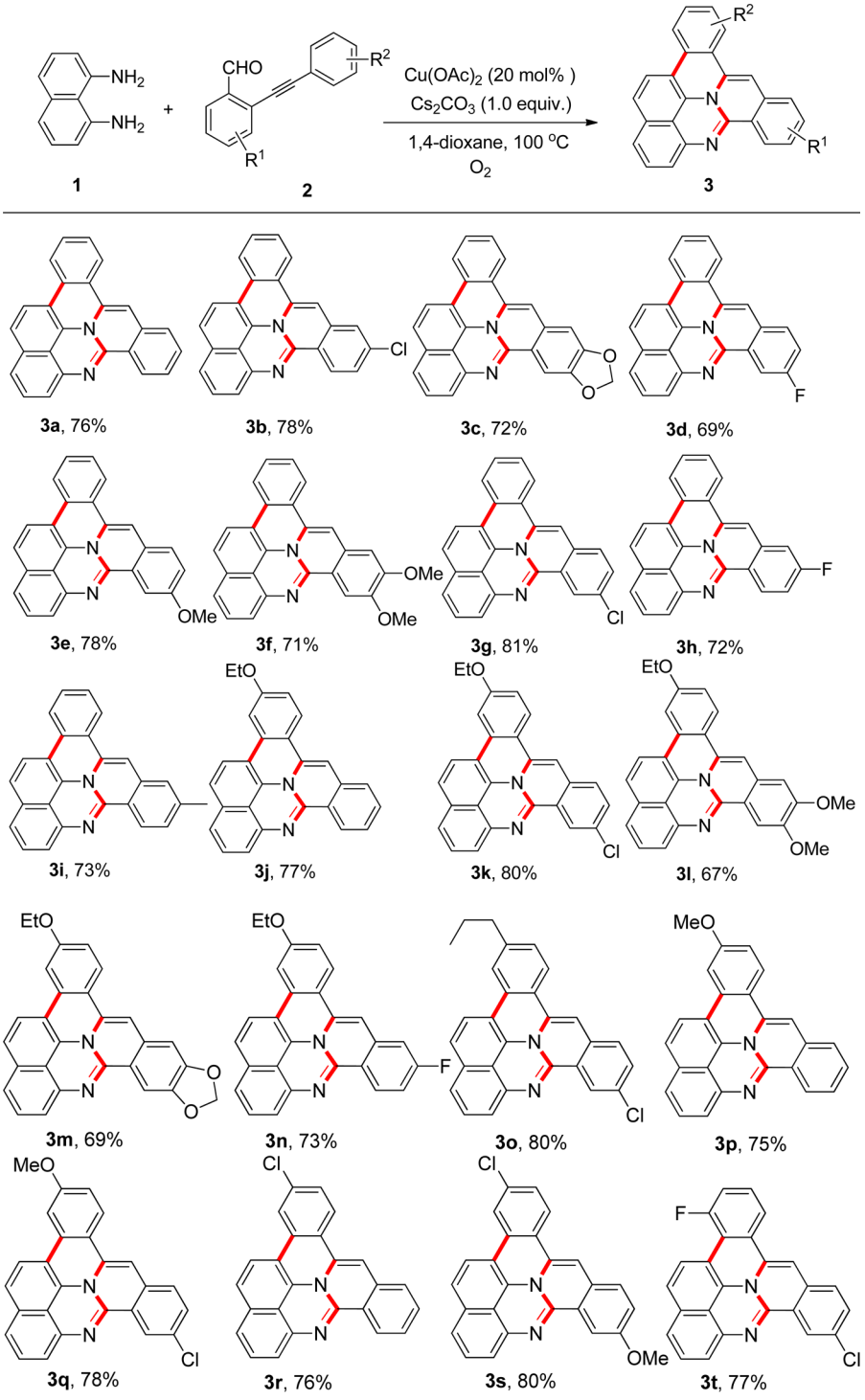
[a]Reagents and conditions: **1** (158 mg, 1.0 mmol), **2a** (206 mg, 1.0 mmol), solvent (10.0 mL), reflux. [b]Base: 1.0 mmol. [c]Isolated yields. [d]130 °C. [e]Reflux.

With the optimized reaction conditions in hand, the reaction scope of this tricyclization was investigated carefully. As shown in Table 2, a wide range of substituted fused quinolizino-[3,4,5,6-*kla*] perimidines **3a**–**s** was synthesized from the corresponding 2-alkynylbenzaldehydes. The benzaldehyde moieties with different functional groups on the benzene ring, including Me, MeO, F, and Cl, were well tolerated under the reaction conditions. The electronic effect of substituents (R^1) has no significant impact on the reaction efficiency. Further, the arylalkynyl moiety with diverse substituent groups (R^2) was explored. It was found that both electron-donating, such as EtO, *n*-Pr, and MeO group, and electron-withdrawing groups (Cl and F atom) on the arylalkynyl moiety were compatible and furnished the expected heptacyclic quinolizino[3,4,5,6-*kla*]perimidines **3j**–**t** with yields ranging from 67% to 80%.

However, 2-(4-nitrophenylethynyl)benzaldehyde with a strong electron-withdrawing group (NO_2) failed to give the desired heptacyclic product instead of leading to the formation of 13-(4-nitrophenyl)isoquinolino[2,1-*a*]perimidine **4u** with a 88% yield under the standard reaction conditions. In addition, when 2-(3-fluorophenylethynyl)-5-chlorobenzaldehyde **2t** was used as the substrate, the product 13-chloro-6-fluorodibenzo-

DOI: 10.1021/acs.joc.6b02644
J. Org. Chem. 2017, 82, 1817–1822

Table 2. Synthetic Results of 3 via Oxidative Coupling and Dehydrogenation[a]



[a]Reagents and conditions: **1** (158 mg, 1.0 mmol), **2** (1.0 mmol), $Cu(OAc)_2$ (36 mg, 0.2 mmol), Cs_2CO_3 (325 mg, 1.0 mmol), dioxane (10.0 mL) under an O_2 balloon, 100 °C.

[1,2:7,8]quinolizino[3,4,5,6-*kla*]perimidine **3t** was obtained in 77% yield with high regioselectivity.

According to the above experimental results (for details, see the Supporting Information) and literature reports,[14] a possible mechanism for forming products **3** is proposed in Scheme 2. The reaction process involves a successive condensation, nucleophilic addition, intramolecular alkyne hydroamination, and oxidative dehydrogenation coupling sequence. The success of this tricyclization is a key oxidative dehydrogenation coupling. Intermediate **7**[11a,16] may be formed through oxidative exchange of $Cu(OAc)_2$ with intermediate product isoquinolino-[2,1-*a*]perimidines **4**. $Cu(OAc)_2$ plausibly performs disproportionation[14] to produce CuOAc, which helps **7** occur oxidative addition to form **8** containing copper(III). The copper(III) inserts the Ar−H bond to yield intermediate **9**, then **9** performs reductive elimination to deliver the final product **3**. Finally, the regeneration of $Cu(OAc)_2$ catalyst to complete the catalytic cycle is by oxidation of O_2.

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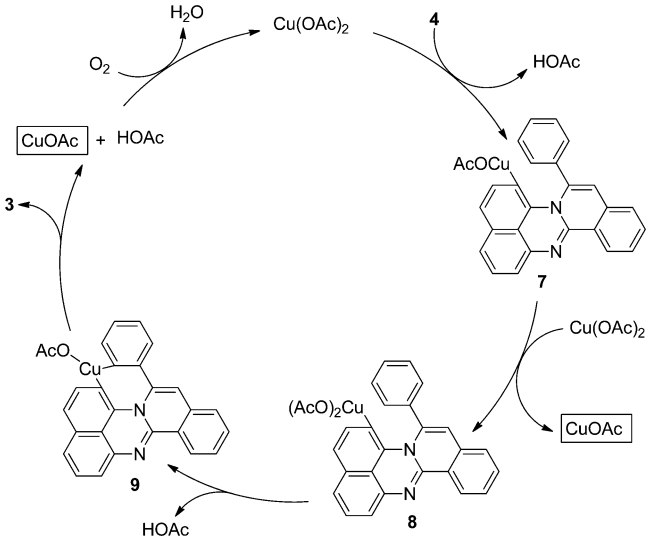
Scheme 2. Possible Reaction Mechanism



In conclusion, we have presented a novel approach for the synthesis of dibenzo[1,2:7,8]quinolizino[3,4,5,6-*kla*]-perimidines catalyzed by $Cu(OAc)_2$ under O_2 conditions. This domino protocol provides a concise access to fused heptacyclic heterocycles bearing quinolizine and perimidine moieties.

EXPERIMENTAL SECTION

General Procedure for the Syntheses of 3. A reaction flask with high vacuum valve was charged with naphthalene-1,8-diamine (158 mg, 1.0 mmol), 2-(arylethynyl)benzaldehyde (1.0 mmol), $Cu(OAc)_2$ (36 mg, 0.2 mmol), and Cs_2CO_3 (325 mg, 1.0 mmol). After the flask was evacuated three times in vacuo and oxygen added, dioxane (10.0 mL) was injected into the mixture. The reaction mixture was then stirred at 100 °C under an O_2 balloon before reaching completion, which was monitored by TLC. The solvent was recovered by distillation under reduced pressure, and the residue was purified by chromatography over silica gel to give **3** using ethyl acetate and petroleum ether (1:16) as an eluent.

Dibenzo[1,2:7,8]quinolizino[3,4,5,6-*kla*]perimidine (3a). Yield: 76% (260 mg). Pale yellow solid. Mp: 122−124 °C (lit.[13] mp 124−126 °C). ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 7.48−7.52 (m, 1H), 7.62−7.69 (m, 3H), 7.77−7.81 (m, 1H), 7.93 (d, J = 9.2 Hz, 1H), 8.14−8.20 (m, 3H), 8.23−8.26 (m, 2H), 8.35 (d, J = 8.0 Hz, 1H), 8.47 (d, J = 8.0 Hz, 1H), 8.64 (d, J = 7.6 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 112.1, 118.2, 121.4, 121.9, 122.3, 122.69, 123.3, 123.4, 124.9, 125.1, 126.4, 127.0, 127.8, 128.2, 128.8, 129.4, 130.1, 130.14, 131.7, 131.8, 133.4, 135.3, 137.2, 140.7, 143.2. IR (KBr): ν 3051, 1707, 1616, 1574, 1547, 1507, 1473, 1423, 1400, 1365, 1301, 1243, 1212, 1170, 1122, 1076, 1009, 821, 791, 754, 691, 658 cm^{-1}. HRMS (TOF, ESI, m/z): calcd for $C_{25}H_{15}N_2$ $[M + H]^+$ 343.1236, found 343.1235.

12-Chlorodibenzo[1,2:7,8]quinolizino[3,4,5,6-*kla*]perimidine (3b). Yield: 78% (294 mg). Pale yellow solid. Mp: 240−242 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 7.50−7.54 (m, 1H), 7.59−7.61 (m, 1H), 7.67−7.71 (m, 2H), 7.93 (d, J = 8.8 Hz, 1H), 8.12−8.15 (m, 2H), 8.18 (d, J = 7.6 Hz, 1H), 8.21−8.28 (m, 3H), 8.46 (d, J = 8.0 Hz, 1H), 8.53 (d, J = 8.0 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 109.8, 112.7, 114.4, 118.3, 120.8, 121.9, 122.0, 122.2, 122.6, 123.0, 123.3, 125.8, 126.49, 126.53, 127.3, 128.1, 128.5, 128.8, 129.6, 130.2, 131.5, 135.0, 138.1, 138.4, 140.7. IR (KBr): ν 3053, 1705, 1609, 1575, 1552, 1509, 1488, 1456, 1419, 1401, 1356, 1320, 1253, 1240, 1215, 1140, 1073, 872, 820, 790, 693, 657 cm^{-1}. HRMS (TOF, ESI, m/z): calcd for $C_{25}H_{14}ClN_2$ $[M + H]^+$ 377.0846, found 377.0833.

[1,3]Dioxolo[4″,5″:4′,5′]benzo[1′,2′:7,8]benzo[1,2]-quinolizino[3,4,5,6-*kla*]perimidine (3c). Yield: 72% (278 mg). Pale yellow solid. Mp: 240−242 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 6.18 (s, 2H), 7.46−7.50 (m, 1H), 7.63−7.67 (m, 2H), 7.71 (s, 1H), 7.91 (d, J = 8.8 Hz, 1H), 7.97 (s, 1H), 8.09−8.13 (m, 2H), 8.16 (d, J = 8.0 Hz, 1H), 8.21 (d, J = 8.8 Hz, 1H), 8.24 (d, J = 8.0 Hz, 1H), 8.43 (d, J = 8.0 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 102.4, 102.5, 104.9, 112.1, 118.2, 121.2, 122.2, 122.6, 122.8, 123.2, 123.7, 124.7, 127.3, 127.4, 127.8, 128.1, 128.8, 129.0, 129.5, 130.1, 133.5, 135.4, 140.6, 143.0, 147.1, 151.5. IR (KBr): ν 2905, 1706, 1614, 1552, 1501, 1462, 1365, 1322, 1260, 1244, 1213, 1174, 1125, 1089, 1034, 935, 893, 821, 790, 754, 691 cm^{-1}. HRMS (TOF, ESI, m/z): calcd for $C_{26}H_{15}N_2O_2$ $[M + H]^+$ 387.1134, found 387.1135.

13-Fluorodibenzo[1,2:7,8]quinolizino[3,4,5,6-*kla*]perimidine (3d). Yield: 69% (249 mg). Pale yellow solid. Mp: 280−282 °C (lit.[13] mp 283−285 °C). ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 7.48−7.53 (m, 2H), 7.65−7.69 (m, 2H), 7.93−7.96 (m, 1H), 8.15−8.19 (m, 3H), 8.23−8.33 (m, 4H), 8.47 (d, J = 8.0 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 112.2 (d, $J_{(F-C)}$ = 24.0 Hz), 112.8, 118.2, 119.0 (d, $J_{(F-C)}$ = 24.0 Hz), 121.5, 122.5, 122.80, 122.82 (d, $J_{(F-C)}$ = 8.0 Hz), 123.1, 123.3, 124.9 (d, $J_{(F-C)}$ = 1.0 Hz), 127.2, 128.0, 128.3, 128.8, 129.5, 130.1, 133.4, 133.5, 135.10(d, $J_{(F-C)}$ = 17.0 Hz), 135.11, 140.5, 148.6, 160.1, 161.3 (d, $J_{(F-C)}$ = 243.0 Hz). IR (KBr): ν 3053, 1792, 1705, 1615, 1573, 1542, 1508, 1473, 1424, 1363, 1321, 1276, 1200, 1122, 1091, 1027, 965, 851, 820, 789, 775, 753, 693 cm^{-1}. HRMS (TOF, ESI, m/z): calcd for $C_{25}H_{14}FN_2$ $[M + H]^+$ 361.1142, found 361.1142.

13-Methoxydibenzo[1,2:7,8]quinolizino[3,4,5,6-*kla*]-perimidine (3e). Yield: 78% (290 mg). Pale yellow solid. Mp: 144−146 °C (lit.[13] mp 140−141 °C). ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 4.01 (s, 3H), 7.30−7.33 (m, 1H), 7.45−7.49 (m, 1H), 7.63−7.67 (m, 2H), 7.90 (d, J = 8.8 Hz, 1H), 8.11−8.15 (m, 4H), 8.19−8.24 (m, 3H), 8.42 (d, J = 7.6 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 56.0, 108.7, 112.8, 118.1, 119.5, 121.1, 122.0, 122.7, 122.7, 123.3, 123.8, 123.9, 127.0, 127.7, 127.9, 128.65, 128.73, 129.4, 130.0, 130.5, 135.1, 135.5, 138.4, 140.5, 143.4, 158.8. IR (KBr): ν 3044, 1772, 1701, 1613, 1558, 1509, 1478, 1457, 1433, 1364, 1322, 1290, 1238, 1214, 1143, 1125, 1105, 1062, 1031, 960, 819, 788, 775, 751, 693 cm^{-1}. HRMS (TOF, ESI, m/z): calcd for $C_{26}H_{17}N_2O$ $[M + H]^+$ 373.1342, found 373.1343.

12,13-Dimethoxydibenzo[1,2:7,8]quinolizino[3,4,5,6-*kla*]-perimidine (3f). Yield: 71% (286 mg). Pale yellow solid. Mp: 229−231 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 4.09 (s, 3H), 4.10 (s, 3H), 7.48−7.51 (m, 1H), 7.65−7.69 (m, 2H), 7.78 (s, 1H), 7.93 (d, J = 8.8 Hz, 1H), 8.09 (s, 1H), 8.14−8.18 (m, 3H), 8.22−8.26 (m, 2H), 8.45 (d, J = 7.6 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 56.3, 56.5, 104.3, 106.9, 112.2, 118.2, 118.7, 118.8, 121.1, 122.1, 122.5, 123.2, 124.0, 124.3, 125.8, 127.3, 127.7, 128.0, 128.7, 129.4, 130.0, 131.8, 135.6, 140.6, 143.4, 148.6, 152.6. IR (KBr): ν 2949, 1769, 1644, 1604, 1579, 1497, 1476, 1455, 1409, 1380, 1331, 1320, 1266, 1223, 1168, 1152, 1113, 1100, 1061, 1008, 824, 799, 768, 721 cm^{-1}. HRMS (TOF, ESI, m/z): calcd for $C_{27}H_{19}N_2O_2$ $[M + H]^+$ 403.1447, found 403.1446.

13-Chlorodibenzo[1,2:7,8]quinolizino[3,4,5,6-*kla*]perimidine (3g). Yield: 81% (305 mg). Pale yellow solid. Mp: 222−224 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 7.47−7.51 (m, 1H), 7.64−7.71 (m, 3H), 7.89 (d, J = 8.8 Hz, 1H), 8.10 (d, J = 7.2 Hz, 2H), 8.12−8.20 (m, 3H), 8.23 (d, J = 8.0 Hz, 1H), 8.42 (d, J = 7.6 Hz, 1H), 8.55 (d, J = 2.0 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 112.6, 118.1, 121.6, 122.3, 122.4, 122.5, 123.0, 123.2, 125.1, 125.2, 126.9, 128.0, 128.3, 128.7, 128.8, 129.4, 129.5, 130.0, 131.5, 132.2, 134.5, 135.0, 135.2, 140.5, 141.9. IR (KBr): ν 3047, 1630, 1601, 1542, 1507, 1492, 1456, 1417, 1403, 1338, 1271, 1245, 1165, 1105, 1070, 1030, 917, 815, 757, 690 cm^{-1}. HRMS (TOF, ESI, m/z): calcd for $C_{25}H_{14}ClN_2$ $[M + H]^+$ 377.0846, found 377.0831.

12-Fluorodibenzo[1,2:7,8]quinolizino[3,4,5,6-*kla*]perimidine (3h). Yield: 72% (259 mg). Pale yellow solid. Mp: >300 °C (lit.[13] mp 298−300 °C). ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 7.31−7.36 (m, 1H), 7.49−7.53 (m, 1H), 7.66−7.70 (m, 2H), 7.93 (d, J = 8.8 Hz, 1H), 7.97−8.00 (m, 1H), 8.12−8.15 (m, 2H), 8.18 (d, J = 8.0 Hz, 1H), 8.23 (d, J = 9.2 Hz, 1H), 8.26 (d, J = 8.0 Hz, 1H), 8.46 (d, J = 7.6 Hz, 1H), 8.58−8.61 (m, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 109.1 (d, $J_{(F-C)}$ = 26.0 Hz), 112.6, 113.8 (d, $J_{(F-C)}$ = 24.0 Hz), 116.2, 118.2, 121.8, 122.5, 122.9, 123.3, 125.7, 126.5(d, $J_{(F-C)}$ = 9.0 Hz), 127.2, 128.1, 128.5, 128.8, 129.3 (d, $J_{(F-C)}$ = 3.0 Hz), 129.6, 130.2, 135.0, 137.4,

DOI: 10.1021/acs.joc.6b02644
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139.2 (d, $J_{(F-C)}$ = 11.0 Hz), 140.7, 142.4, 153.6, 165.2 (d, $J_{(F-C)}$ = 250.0 Hz). IR (KBr): ν 3058, 1706, 1684, 1618, 1568, 1508, 1470, 1457, 1424, 1405, 1327, 1296, 1260, 1242, 1192, 1132, 1077, 1003, 892, 864, 837, 820, 791, 773, 753 cm^{-1}. HRMS (TOF, ESI, m/z): calcd for $C_{25}H_{14}FN_2$ $[M + H]^+$ 361.1142, found 361.1143.

12-Methyldibenzo[1,2:7,8]quinolizino[3,4,5,6-*kla*]-perimidine (3i). Yield: 73% (260 mg). Pale yellow solid. Mp: 129−131 °C (lit.[13] mp 128−130 °C). ^1H NMR ($CDCl_3$, 400 MHz): δ_H 2.59 (s, 3H), 7.38 (d, J = 8.0 Hz, 1H), 7.46−7.50 (m, 1H), 7.64−7.68 (m, 2H), 7.87 (d, J = 8.8 Hz, 1H), 8.06 (s, 1H), 8.09−8.20 (m, 5H), 8.39−8.45 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 22.5, 112.7, 118.1, 121.3, 122.1, 122.4, 122.5, 123.2, 123.3, 124.6, 124.7, 126.9, 127.5, 127.7, 128.1, 128.8, 129.4, 130.0, 130.79, 130.83, 135.4, 137.5, 140.7, 142.6, 143.2, 148.2. IR (KBr): ν 3025, 2924, 2845, 1648, 1632, 1611, 1587, 1508, 1496, 1475, 1447, 1390, 1370, 1262, 1211, 1179, 1152, 1100, 1010, 810, 749, 735, 705, 663, 635 cm^{-1}. HRMS (TOF, ESI, m/z): calcd for $C_{26}H_{17}N_2$ $[M + H]^+$ 357.1392, found 357.1399.

7-Ethoxydibenzo[1,2:7,8]quinolizino[3,4,5,6-*kla*]perimidine (3j). Yield: 77% (298 mg). Pale yellow solid. Mp: 222−224 °C. ^1H NMR ($CDCl_3$, 400 MHz): δ_H 1.52 (t, J = 7.2 Hz, 3H), 4.20 (q, J = 7.2 Hz, 2H), 7.20 (d, J = 8.4 Hz, 2H), 7.62−7.66 (m, 1H), 7.78−7.82 (m, 1H), 7.94 (d, J = 9.2 Hz, 1H), 8.11−8.14 (m, 2H), 8.18 (d, J = 8.0 Hz, 1H), 8.23−8.27 (m, 2H), 8.36 (d, J = 8.0 Hz, 1H), 8.47 (d, J = 7.6 Hz, 1H), 8.66 (d, J = 7.6 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 14.9, 63.7, 111.0, 112.9, 114.2, 115.5, 115.6, 118.1, 121.3, 121.8, 122.1, 122.5, 123.4, 125.1, 125.2, 126.2, 127.7, 128.2, 130.1, 130.2, 131.7, 132.3, 133.3, 137.3, 140.9, 143.3, 158.9. IR (KBr): ν 3054, 2925, 1678, 1599, 1508, 1475, 1420, 1392, 1248, 1172, 1115, 1042, 991, 943, 921, 822, 757, 691 cm^{-1}. HRMS (TOF, ESI, m/z): calcd for $C_{27}H_{19}N_2O$ $[M + H]^+$ 387.1498, found 387.1497.

13-Chloro-7-ethoxydibenzo[1,2:7,8]quinolizino[3,4,5,6-*kla*]-perimidine (3k). Yield: 80% (337 mg). Pale yellow solid. Mp: 225−227 °C. ^1H NMR ($CDCl_3$, 400 MHz): δ_H 1.52 (t, J = 7.2 Hz, 3H, CH_3), 4.20 (q, J = 7.2 Hz, 2H, CH_2), 7.19 (d, J = 8.8 Hz, 2H), 7.72−7.74 (m, 1H), 7.92 (d, J = 9.2 Hz, 1H), 8.07 (d, J = 8.8 Hz, 2H), 8.15−8.26 (m, 4H), 8.45 (d, J = 8.0 Hz, 1H), 8.60 (d, J = 2.0 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 14.9, 63.7, 112.8, 115.5, 118.1, 121.5, 122.1, 122.35, 122.42, 122.8, 123.3, 125.2, 125.7, 126.3, 127.3, 127.4, 128.37, 128.41, 130.1, 130.2, 131.6, 132.0, 134.5, 135.4, 137.7, 140.8, 159.1. IR (KBr): ν 3049, 2977, 1635, 1604, 1577, 1522, 1508, 1476, 1458, 1395, 1372, 1280, 1247, 1173, 1138, 1153, 1073, 1043, 941, 922, 821, 795, 761, 693, 641 cm^{-1}. HRMS (TOF, ESI, m/z): calcd for $C_{27}H_{18}ClN_2O$ $[M + H]^+$ 421.1108, found 421.1107.

7-Ethoxy-12,13-dimethoxydibenzo[1,2:7,8]quinolizino-[3,4,5,6-*kla*]perimidine (3l). Yield: 67% (299 mg). Pale yellow solid. Mp: 233−235 °C. ^1H NMR ($CDCl_3$, 400 MHz): δ_H 1.52 (t, J = 7.2 Hz, 3H), 4.10 (s, 3H), 4.12 (s, 3H), 4.20 (q, J = 7.2 Hz, 2H), 7.20 (d, J = 8.8 Hz, 2H), 7.79 (s, 1H), 7.93 (d, J = 8.8 Hz, 1H), 8.09−8.14 (m, 3H), 8.17 (d, J = 8.0 Hz, 1H), 8.22−8.26 (m, 2H), 8.45 (d, J = 8.0 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 14.9, 56.3, 56.5, 63.7, 112.3, 112.8, 115.2, 115.47, 115.54, 118.0, 118.9, 120.9, 121.4, 122.3, 122.6, 122.7, 122.8, 123.2, 123.4, 125.2, 127.4, 128.0, 128.3, 129.9, 130.0, 131.9, 133.6, 152.7, 159.0. IR (KBr): ν 3041, 2927, 1682, 1638, 1605, 1579, 1500, 1462, 1379, 1321, 1266, 1168, 1119, 1099, 1073, 1026, 942, 825, 767, 747, 703, 668 cm^{-1}. HRMS (TOF, ESI, m/z): calcd for $C_{29}H_{23}N_2O_3$ $[M + H]^+$ 447.1709, found 447.1705.

7-Ethoxy[1,3]dioxolo[4″,5″:4′,5′]benzo[1′,2′:7,8]benzo[1,2]-quinolizino[3,4,5,6-*kla*]perimidine (3m). Yield: 69% (297 mg). Pale yellow solid. Mp: 240−242 °C. ^1H NMR ($CDCl_3$, 400 MHz): δ_H 1.52 (t, J = 7.2 Hz, 3H), 4.19 (q, J = 7.2 Hz, 2H), 6.21 (s, 2H), 7.19 (d, J = 8.8 Hz, 2H), 7.75 (s, 1H), 7.92 (d, J = 8.8 Hz, 1H), 8.00−8.07 (m, 3H), 8.14−8.26 (m, 3H), 8.45 (d, J = 7.6 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 14.9, 63.7, 102.2, 102.4, 104.8, 114.3, 114.7, 115.5, 117.9, 121.0, 122.0, 122.3, 123.2, 123.2, 125.0, 127.1, 127.7, 128.1, 130.0, 130.1, 130.6, 133.1, 133.5, 140.6, 142.9, 146.9, 151.4, 158.9. IR (KBr): ν 3045, 2975, 1636, 1602, 1579, 1508, 1466, 1401, 1371, 1333, 1291, 1259, 1245, 1174, 1113, 1036, 928, 877, 822, 759, 720, 680 cm^{-1}. HRMS (TOF, ESI, m/z): calcd for $C_{28}H_{19}N_2O_3$ $[M + H]^+$ 431.1396, found 431.1381.

7-Ethoxy-12-fluorodibenzo[1,2:7,8]quinolizino[3,4,5,6-*kla*]-perimidine (3n). Yield: 73% (295 mg). Pale yellow solid. Mp: 276−278 °C. ^1H NMR ($CDCl_3$, 400 MHz): δ_H 1.53 (t, J = 6.8 Hz, 3H), 4.20 (q, J = 6.8 Hz, 2H), 7.19−7.22 (m, 2H), 7.30−7.35 (m, 1H), 7.93 (d, J = 8.8 Hz, 1H), 7.96−7.99 (m, 1H), 8.05−8.09 (m, 2H), 8.15−8.26 (m, 3H), 8.45 (d, J = 8.0 Hz, 1H), 8.59−8.62 (m, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 14.9, 63.8, 108.9 (d, $J_{(F-C)}$ = 25.0 Hz), 112.6, 113.6 (d, $J_{(F-C)}$ = 24.0 Hz), 115.6, 115.7, 118.0, 121.6, 122.1, 122.3, 122.6, 123.3, 126.0, 126.5 (d, $J_{(F-C)}$ = 11.0 Hz), 127.4 (d, $J_{(F-C)}$ = 11.0 Hz), 128.4, 129.2 (d, $J_{(F-C)}$ = 2.0 Hz), 130.1, 130.3, 139.2, 139.3, 140.9, 142.4, 159.1, 164.5, 165.2 (d, $J_{(F-C)}$ = 250.0 Hz). IR (KBr): ν 3058, 2985, 2930, 1635, 1618, 1603, 1511, 1496, 1476, 1435, 1416, 1393, 1333, 1308, 1286, 1253, 1230, 1117, 1063, 1045, 989, 963, 945, 899, 870, 839, 801, 653 cm^{-1}. HRMS (TOF, ESI, m/z): calcd for $C_{27}H_{18}FN_2O$ $[M + H]^+$ 405.1404, found 405.1405.

13-Chloro-7-propyldibenzo[1,2:7,8]quinolizino[3,4,5,6-*kla*]-perimidine (3o). Yield: 80% (335 mg). Pale yellow solid. Mp: 241−243 °C. ^1H NMR ($CDCl_3$, 400 MHz): δ_H 1.06 (t, J = 7.2 Hz, 3H), 1.79 (q, J = 7.6 Hz, 2H), 2.75 (t, J = 7.6 Hz, 2H), 7.48 (d, J = 8.4 Hz, 2H), 7.71−7.74 (m, 1H), 7.92 (d, J = 8.8 Hz, 1H), 8.05 (d, J = 8.0 Hz, 2H), 8.14−8.18 (m, 1H), 8.21−8.26 (m, 3H), 8.45 (d, J = 7.6 Hz, 1H), 8.59 (d, J = 2.0 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 14.0, 24.6, 38.0, 112.7, 118.2, 121.5, 122.2, 122.4, 122.5, 122.9, 123.4, 125.1, 125.6, 127.1, 128.3, 128.4, 128.7, 128.8, 129.6, 130.1, 131.5, 132.1, 132.4, 134.5, 135.4, 140.6, 142.0, 142.9. IR (KBr): ν 3053, 2956, 2928, 1602, 1507, 1484, 1448, 1417, 1362, 1266, 1177, 1114, 1075, 941, 880, 818, 793, 755, 692 cm^{-1}. HRMS (TOF, ESI, m/z): calcd for $C_{28}H_{20}ClN_2$ $[M + H]^+$ 419.1316, found 419.1322.

7-Methoxydibenzo[1,2:7,8]quinolizino[3,4,5,6-*kla*]-perimidine (3p). Yield: 75% (279 mg). Pale yellow solid. Mp: 220−222 °C. ^1H NMR ($CDCl_3$, 400 MHz): δ_H 3.95 (s, 3H), 7.17 (d, J = 8.4 Hz, 2H), 7.55−7.59 (m, 1H), 7.71−7.74 (m, 1H), 7.84 (d, J = 9.2 Hz, 1H), 8.06 (d, J = 8.8 Hz, 2H), 8.09−8.19 (m, 3H), 8.25 (d, J = 8.0 Hz, 1H), 8.41 (d, J = 7.6 Hz, 1H), 8.58 (d, J = 7.6 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 55.5, 112.7, 114.9, 117.9, 121.2, 121.7, 122.0, 122.4, 122.8, 123.2, 124.9, 125.0, 126.1, 127.0, 127.8, 128.1, 130.0, 130.1, 131.6, 131.8, 133.2, 137.2, 140.7, 143.0, 143.8, 159.4. IR (KBr): ν 3011, 2917, 1608, 1548, 1523, 1507, 1474, 1462, 1427, 1393, 1366, 1326, 1293, 1252, 1173, 1112, 1025, 842, 820, 788, 754, 709, 692, 658, 618 cm^{-1}. HRMS (TOF, ESI, m/z): calcd for $C_{26}H_{17}N_2O$ $[M + H]^+$ 373.1342, found 373.1347.

13-Chloro-7-methoxydibenzo[1,2:7,8]quinolizino[3,4,5,6-*kla*]perimidine (3q). Yield: 78% (317 mg). Pale yellow solid. Mp: 225−227 °C. ^1H NMR ($CDCl_3$, 400 MHz): δ_H 3.96 (s, 3H), 7.16 (d, J = 8.8 Hz, 2H), 7.63−7.66 (m, 1H), 7.82 (d, J = 8.8 Hz, 1H), 7.98 (d, J = 8.8 Hz, 2H), 8.08−8.12 (m, 3H), 8.17 (d, J = 7.6 Hz, 1H), 8.37 (d, J = 8.0 Hz, 1H), 8.49 (d, J = 1.6 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 55.5, 112.6, 115.0, 117.9, 121.4, 121.8, 122.2, 122.3, 122.8, 123.2, 123.5, 125.1, 125.4, 127.0, 127.5, 128.3, 130.0, 130.1, 131.4, 131.9, 134.3, 135.2, 140.6, 141.8, 142.7, 159.6. IR (KBr): ν 3067, 1723, 1636, 1604, 1577, 1509, 1459, 1440, 1395, 1375, 1321, 1279, 1250, 1205, 1182, 1138, 1107, 1075, 1057, 1027, 940, 877, 830, 794, 761 cm^{-1}. HRMS (TOF, ESI, m/z): calcd for $C_{26}H_{16}ClN_2O$ $[M + H]^+$ 407.0951, found 407.0945.

7-Chlorodibenzo[1,2:7,8]quinolizino[3,4,5,6-*kla*]perimidine (3r). Yield: 76% (286 mg). Pale yellow solid. Mp: 223−225 °C. ^1H NMR ($CDCl_3$, 400 MHz): δ_H 7.61−7.65 (m, 3H), 7.76−7.80 (m, 1H), 7.91 (d, J = 8.8 Hz, 1H), 8.07 (d, J = 8.4 Hz, 2H), 8.13−8.17 (m, 2H), 8.23−8.27 (m, 2H), 8.45 (d, J = 7.6 Hz, 1H), 8.62 (d, J = 7.6 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 104.9, 112.7, 118.0, 121.6, 121.8, 122.5, 122.87, 122.92, 123.4, 123.5, 123.6, 125.2, 126.6, 126.9, 128.3, 129.6, 129.9, 130.0, 131.8, 133.3, 133.6, 133.8, 136.9, 140.6, 143.1. IR (KBr): ν 3239, 1636, 1616, 1588, 1521, 1516, 1507, 1488, 1473, 1418, 1396, 1349, 1091, 835, 787, 757, 701, 668 cm^{-1}. HRMS (TOF, ESI, m/z): calcd for $C_{25}H_{14}ClN_2$ $[M + H]^+$ 377.0846, found 377.0841.

7-Chloro-13-methoxydibenzo[1,2:7,8]quinolizino[3,4,5,6-*kla*]perimidine (3s). Yield: 80% (325 mg). Pale yellow solid. Mp: 238−240 °C. ^1H NMR ($CDCl_3$, 400 MHz): δ_H 4.04 (s, 3H), 7.34−7.37 (m, 1H), 7.62 (d, J = 8.4 Hz, 2H), 7.94 (d, J = 8.8 Hz, 1H), 8.09

DOI: 10.1021/acs.joc.6b02644
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(d, J = 8.0 Hz, 2H), 8.14−8.21 (m, 4H), 8.27 (d, J = 7.6 Hz, 1H), 8.46 (d, J = 8.0 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 56.0, 108.9, 109.9, 112.8, 118.0, 119.6, 121.3, 122.3, 122.5, 122.6, 122.9, 123.0, 127.05, 127.06, 128.1, 128.2, 129.6, 129.7, 130.00, 130.02, 130.3, 133.5, 134.1, 135.1, 140.5, 159.0. IR (KBr): ν 3239, 1771, 1733, 1637, 1616, 1583, 1558, 1540, 1507, 1478, 1434l, 1289, 1236, 1213, 1124, 1092, 1062, 851, 820, 810, 786, 708, 668 cm^{-1}. HRMS (TOF, ESI, m/z): calcd for $C_{26}H_{16}ClN_2O$ $[M + H]^+$ 407.0952, found 407.0958.

13-Chloro-6-fluorodibenzo[1,2:7,8]quinolizino[3,4,5,6-*kla*]-perimidine (3t). Yield: 77% (304 mg). Pale yellow solid. Mp: 234−236 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 7.17−7.22 (m, 1H), 7.60−7.62 (m, 1H), 7.74−7.77 (m, 1H), 7.79−7.82 (m, 1H), 7.91 (d, J = 7.6 Hz, 1H), 7.95 (d, J = 8.8 Hz, 1H), 8.16−8.23 (m, 3H), 8.28 (d, J = 7.6 Hz, 1H), 8.47 (d, J = 8.0 Hz, 1H), 8.60 (d, J = 2.0 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 112.7, 114.8 (d, $J_{(F-C)}$ = 21.0 Hz), 115.4 (d, $J_{(F-C)}$ = 22.0 Hz), 118.2, 122.0, 122.6, 122.8, 122.9 (d, $J_{(F-C)}$ = 8.0 Hz), 123.4, 124.4 (d, $J_{(F-C)}$ = 3.0 Hz), 124.5, 125.3, 127.0, 128.5, 130.1, 131.1 (d, $J_{(F-C)}$ = 8.0 Hz), 131.8, 132.6, 134.6, 135.1, 137.25, 137.33, 140.5, 142.1, 163.5 (d, $J_{(F-C)}$ = 245.0 Hz). IR (KBr): ν 3071, 1685, 1635, 1616, 1600, 1561, 1492, 1470, 1441, 1380, 1342, 1302, 1269, 1239, 1189, 1154, 1106, 1026, 918, 880, 868, 866, 796, 763, 731, 695 cm^{-1}. HRMS (TOF, ESI, m/z): calcd for $C_{25}H_{13}ClFN_2$ $[M + H]^+$ 395.0752, found 395.0744.

13-(4-Nitrophenyl)isoquinolino[2,1-*a*]perimidine (4u). Yield: 88% (343 mg). Red solid. Mp: 227−229 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 5.48 (d, J = 7.6 Hz, 1H), 6.88−6.92 (m, 1H), 7.00 (s, 1H), 7.05 (d, J = 8.4 Hz, 2H), 7.32 (d, J = 8.0 Hz, 1H), 7.42−7.44 (m, 1H), 7.51−7.54 (m, 2H), 7.60−7.66 (m, 1H), 7.69−7.74 (m, 1H), 7.96 (d, J = 8.0 Hz, 1H), 8.10 (d, J = 8.8 Hz, 2H), 8.22 (d, J = 7.6 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 104.5, 111.4, 119.3, 119.7, 120.1, 121.4, 122.7, 122.9, 123.4, 124.1, 125.6, 128.1, 129.1, 129.7, 130.5, 131.1, 132.0, 134.4, 135.7, 138.5, 141.0, 145.6, 152.9. IR (KBr): ν 3053, 1640, 1622, 1573, 1517, 1508, 1474, 1378, 1341, 1222, 1181, 1104, 1060, 872, 825, 774, 755, 688 cm^{-1}. HRMS (TOF, ESI, m/z): calcd for $C_{25}H_{16}N_3O_2$ $[M + H]^+$ 390.1243, found 390.1255.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b02644.

Data and ^{1}H and ^{13}C NMR spectra for compounds **3a−t**, **4a**,**u**, and **5k** (PDF)

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We are grateful to the Major Natural Science Foundation of Jiangsu Province (14KJA150004), a project funded by the Priority Academic Program Development of Jiangsu Higher Education Institutions of Jiangsu Province, for financial support.

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DOI: 10.1021/acs.joc.6b02644
J. Org. Chem. 2017, 82, 1817−1822