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Site-Selective Electrophilic Cyclization and Subsequent Ring-Opening: A Synthetic Route to Pyrrolo[1,2-*a*]quinolines and Indolizines

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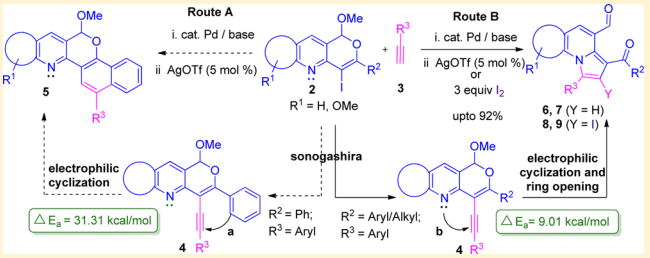
Supporting Information

ABSTRACT: An efficient strategy for the synthesis of pyrrolo[1,2-*a*]quinolines and indolizines from pyranoquinolines via site-selective electrophilic cyclization and subsequent opening of pyran ring using silver/iodine under mild reaction conditions is described. This approach involves the preferential attack of the pyridyl nitrogen over aryl ring and leads to the formation of 5-*endo-dig* cyclized products. Quantum chemical calculations between C−N (ΔE_a = 9.01 kcal/mol) and C−C (ΔE_a = 31.31 kcal/mol) bond formation were performed in order to rationalize the observed site selectivity. Structure of the products were confirmed by the X-ray crystallographic studies. Iodo-substituted compounds generated by the electrophilic iodocyclization were further diversified via Pd-catalyzed cross-coupling reactions.



INTRODUCTION

The simplicity, efficiency and generality of the transition-metal-catalyzed tandem reactions[1] have led to its applications in the synthesis of a wide variety of heterocyclic/carbocyclic compounds and natural products. Nitrogen-containing heterocycles and their analogues are pharmaceutically important scaffolds.[2] During the past decade, pharmacological prospectives of the pyrrolo[1,2-*a*]quinolines[3] and indolizines[4] has been well recognized due to their potential biological activity and presence in many natural alkaloids. Some of the pyrrole-fused heterocycles, such as dihydroisoquinolines, have shown in vivo activity against P388 leukemia[5] (Figure 1). The nucleus of indolizine derivatives are associated with a wide range of biological activities including anticancer,[6] antibacterial,[3a] antifungal,[7] antitubercular[8] and antihistaminic,[9] cytotoxic and CNS depressant activity[10] (Figure 1).

Although numerous methods are available for the synthesis of pyrrolo[1,2-*a*]quinoline[11] and indolizines,[12] new strategies to synthesize these classes of scaffolds with high molecular diversity are highly in demand. Halogenated heterocyclic compounds serve as a useful platform for increasing the molecular diversity.[13] In this context, the reactions incorporating halogens like iodocyclization[14,15] are highly valuable. The introduction of iodide functionality in the molecule provides avenues for further synthetic elaboration.

In 2007, Gevergyon and co-workers[16] reported the synthesis of pyrroloquinolines and indolizines by the metal-catalysis (Scheme 1, eq 1), while recently Kim and co-workers[17] reported the synthesis of indolizines by 5-*endodig* iodocyclization (Scheme 1, eq 2). To the best of our knowledge, cyclization followed by ring-opening has not been explored. Herein, we reported the synthesis of highly functionalized pyrrolo[1,2-*a*]quinoline and indolizines via silver-catalyzed as well as iodine-mediated 5-*endodig* cyclization with successive ring-opening under mild reaction conditions (Scheme 2).

RESULTS AND DISCUSSION

Previously, Larock and co-workers reported the synthesis of fused polycyclic compounds via palladium-catalyzed annulations, which involved the electrophilic cyclization through the CH activation of adjacent aromatic carbon.[18] As a part of our ongoing efforts in the synthesis of heterocycles[19] by electrophilic cyclization of alkynes,[20] we hypothesized the synthesis of polyheterocycles **5** from alkynyl pyranoquinoline **4** by C−C bond formation under proper reaction conditions (Scheme 2, route A).

Our initial studies showed that reaction failed to afford the designed heterocycle **5**; however, a novel product **6a** was isolated (Scheme 2, route B). The structure of the product **6a** was unambiguously established as pyrrolo[1,2-*a*]quinoline by the X-ray crystallographic analysis[21] (see Supporting Information Figure S1). Efforts to synthesize **6a** directly from 4-iodopyranoquinoline **2a** require high catalyst loading and

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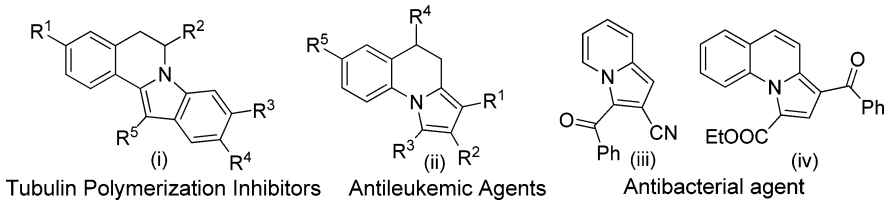
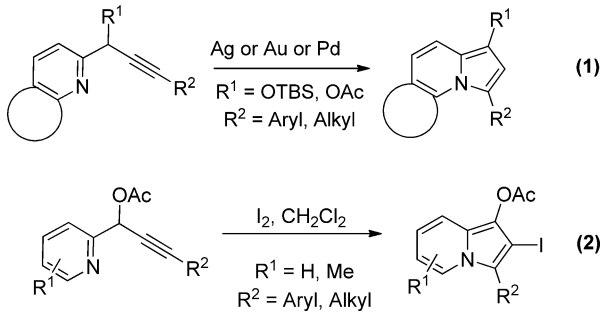


Figure 1. Selected examples of biologically relevant pyrrolo-quinolines and indolizines.

Scheme 1. Synthesis of Pyrroloquinolines and Indolizines[a]



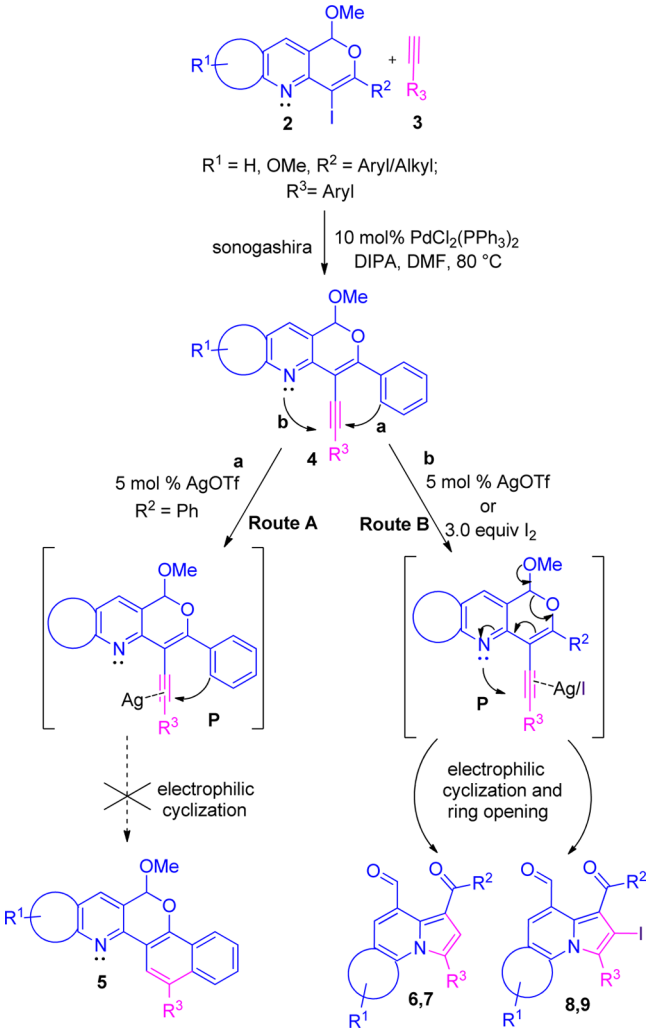
[a](1) Metal-catalyzed synthesis of pyrrolo[1,2-a]quinolines and indolizines by Gevorgyan and co-workers. (2) Iodine-mediated synthesis of indolizines by Kim and co-workers.

afforded the product **6a** in low yield. The possible reason might be due to the formation of iodo reduced[22] product. This developed methodology provides heterocycles with two carbonyl groups, which could be useful for the medicinal utility of the molecule.[4e]

To identify the optimal conditions for the reaction, a number of reported catalysts for cyclization such as Ag(I), Cu(I), Pd(II) and I_2 along with several organic solvents were examined in the reaction of 1-methoxy-3-phenyl-4-(phenylethynyl)-1*H*-pyrano-[4,3-*b*]quinoline (**4a**) under various conditions (Table 1). When 5 mol % of $Pd(OAc)_2$ were used as catalyst in CH_2Cl_2, no consumption of substrate **4a** was observed after 5 h (Table 1, entry 1). Increasing the catalyst loading from 5 to 10 mol % made no effect on the substrate **4a** even after 10 h (entry 2). $PdCl_2(PPh_3)_2$ and CuI were also found ineffective for the reaction (entries 3 and 4). When Ag(I) salts like AgOTf was used, surprisingly product **6a** was obtained in 90% yield (entry 5). Decreasing the catalyst loading from 10 to 5 mol % made no considerable effect on the yield of product **6a**, and the reaction was completed in 3 h (entries 6 and 7). Decrease in the catalyst loading from 5 to 2 mol % adversely effected the yield of the product **6a** (entry 8). Longer reaction time also lead to the incomplete conversion of **4a** and afforded the product **6a** in 55% yield only (entry 9). From entries 9−13 in Table 1, it is apparent that solvent has a significant influence on the reaction. CH_2Cl_2 and $CHCl_3$ were found suitable for this reaction, and THF afforded the product **6a** in lower yield (entries 10 and 11), while no reaction was observed in protic solvents like EtOH and H_2O (entries 12 and 13). Other silver catalysts like AgOAc and $AgNO_3$ were found effective and afforded the product **6a** in 60 and 78% yields, respectively (entries 14 and 15). After screening various metal catalysts, Ag(I) catalyst was found to be most efficient to carry out this transformation.

After optimizing the reaction conditions with metal catalysts, we next examined the efficacy of iodine for this reaction. Use of a catalytic amount of iodine was found ineffective (entry 16); however 1.0 equiv of iodine afforded the 2-iodopyrrolo[1,2-a]quinoline **8a** in 45% yield (entry 17). With 2.0 equiv of iodine, product **8a** was obtained in 70% yield (entry 18), while 3.0 equiv of iodine afforded the product **8a** in 85% yield with in 3 h (entry 19). A longer reaction time made no significant changes in the yield of product **8a** (entry 20).

Scheme 2. Design of Tandem Strategy for the Synthesis of Heterocycles 5−9



We then investigated the substrate scope of the developed chemistry (Table 2). The substrate 4-alkynyl-pyrano[4,3-*b*]quinolines **4a−o** and pyrano[4,3-*b*]pyridine **4p−t** required for examining the scope of the reaction were readily prepared by the Sonogashira coupling of the 4-iodopyrano[4,3-*b*]-quinolines **2a−j** with terminal alkynes **3**. The substrates **2a−j** required for this approach were readily prepared by electrophilic iodocyclization of *ortho*-alkynylaldehydes using reported procedure (Scheme 3).[15b,c]

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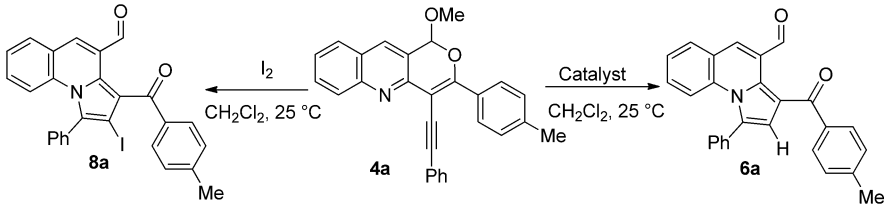
Table 1. Optimization of the Reaction Conditions[a]



entry	solvent	catalyst	mol %	t (h)	yield[b] 6a	yield[b] 8a
1	CH_2Cl_2	$Pd(OAc)_2$	5	5	00	
2	CH_2Cl_2	$Pd(OAc)_2$	10	10	00	
3	CH_2Cl_2	$PdCl_2(PPh_3)_2$	10	10	00	
4	CH_2Cl_2	CuI	10	10	00	
5	CH_2Cl_2	AgOTf	10	5	90	
6	CH_2Cl_2	AgOTf	5	5	90	
7	**CH_2Cl_2**	**AgOTf**	**5**	**3**	**90**	
8	CH_2Cl_2	AgOTf	2	3	45	
9	CH_2Cl_2	AgOTf	2	5	55	
10	$CHCl_3$	AgOTf	5	3	86	
11	THF	AgOTf	5	3	75	
12	EtOH	AgOTf	5	3	00	
13	H_2O	AgOTf	5	3	00	
14	CH_2Cl_2	AgOAc	5	3	60	
15	CH_2Cl_2	$AgNO_3$	5	3	78	
16	CH_2Cl_2	I_2	10	3		
17	CH_2Cl_2	I_2	1[c]	3		45
18	CH_2Cl_2	I_2	2[c]	3		70
19	**CH_2Cl_2**	**I_2**	**3**[c]	**3**		**81**
20	CH_2Cl_2	I_2	3[c]	10		81

[a]Reactions were performed using 0.25 mmol of **4a**, catalyst in 2.0 mL of solvent at 25 °C unless otherwise noted. [b]Isolated yield. [c]Equiv.

As shown in Table 2, the reaction was well tolerant toward a variety of R^1, R^2 and R^3 substituents (entries 1−20). Substrates bearing aryl group at R^2 afforded the desired product **6a−l**, **6o** in good to excellent yields (entries 1−12, 15). However, aliphatic substituents afforded the desired products **6m** and **6n** in lower yields and required longer reaction time (entries 13 and 14). The substrates **4m**,**n** with aliphatic substituents were unstable; therefore, they were used directly for the reaction without isolation. Alkynes bearing an electron-rich substituents at R^3 provided the desired products **6b**,**c**, **6e−g**, **6i−k** in 82−92% yield (entries 2−3, 5−7, 9−11). However, substrates **4h** and **4l** having *n*-alkyl substituted aryl group at R^3 afforded the products **6h** and **6l** in comparatively lower yields (entries 8 and 12). The presence of OMe group at R^1 made no significant effect on the yield of the desired product **6o** (entry 15). To further examine the generality of the developed chemistry, pyrano[4,3-*b*]pyridines **4p−t** were allowed to react under the optimized reaction conditions (entries 16−20). The electron-deficient aromatic ring of this substrate afforded the corresponding indolizines **7a−e** in 75−80% yields. No significant effect on the yield of the product **7a** was observed with substrate **4p** having meta substituted aryl alkyne at R^3 (entry 16).

After obtaining successful results with Ag(I) catalyst, we have further extended the scope of this chemistry by employing iodine as an electrophile. To our delight, this electrophilic cyclization proceeded smoothly and afforded the iodo products **8a−j** and **9a**,**b** in good yields (Table 3). Substrate with electron-rich substitutents afforded the corresponding products **8a−h**, **8j** in 75−84% yields (entries 1−8, 10), while product **8i** was obtained in 70% yield with alkyne **4n** bearing cyclohexyl group at R^2 (entry 9). Iodo-indolizines **9a**,**b** were obtained in 72−75% yields using alkynes **4q** and **4s** (entries 11 and 12).

The formation of the desired iodocyclized compounds **8a−j** and **9a**,**b** were confirmed by their spectral data (^{1}HNMR, ^{13}CNMR and HRMS) and finally by the X-ray crystallographic data of compound **9b**[21] (see Supporting Information Figure S2).

To rationalize this tandem process, we proposed a plausible mechanism (Scheme 4). Presumably, the Ag metal coordinates with the triple bond of alkyne **4** to form intermediate **P**; similarly, iodine forms iodonium intermediate **P′**. The formation of intermediate **P** and **P′** triggers the attack of pyridyl nitrogen on the triple bond, which leads to the generation of cationic species **Q** and **Q′** via intramolecular 5-*endodig* cyclization.[16b] The cationic species **Q** and **Q′** then aromatize to form the oxonium intermediate **R**. Because of the instability of the intermediate **R**, it immediately converts into a more stable intermediate **S** by opening of pyran ring, which upon loss of the Me[18c] and MeI[13f] provided the product **6**, **7** and **8**, **9** respectively. Loss of the Me group is thought to occur during the aqueous workup, but the actual path for this step is unclear.

With above results, we investigated further structural elaboration of the iodo-substituted pyrrolo[1,2-*a*]quinolines via palladium-catalyzed cross-coupling reactions. To this end, compound **8a** was functionalized by applying palladium-catalyzed Suzuki[23] and Heck[24] coupling reactions to afford

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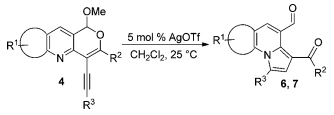
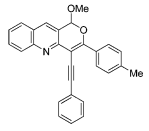
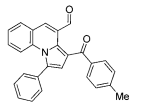
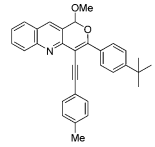
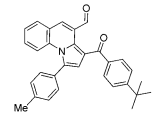
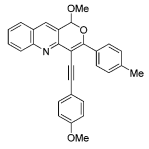
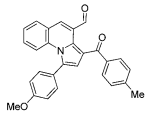
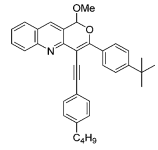
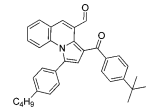
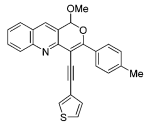
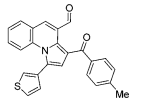
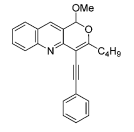
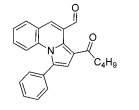
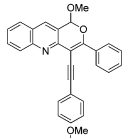
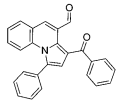
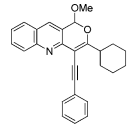
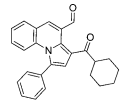
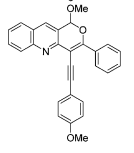
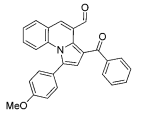
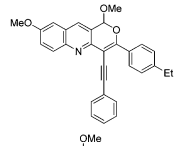
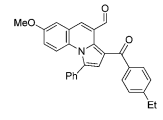
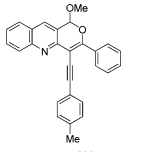
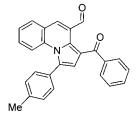
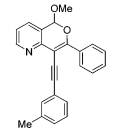
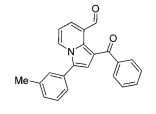
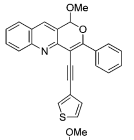
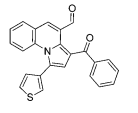
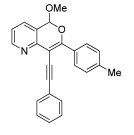
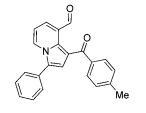
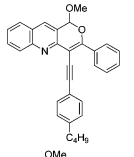
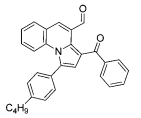
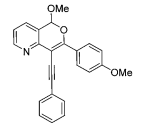
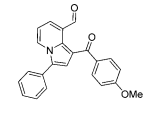
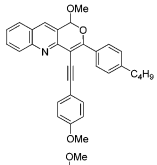
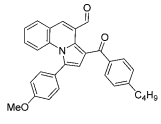
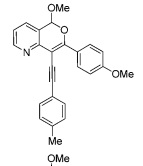
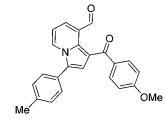
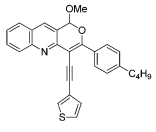
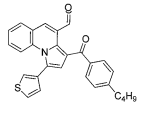
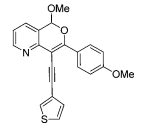
Table 2. Scope of the Developed Tandem Strategy for the Synthesis of Pyrrolo[1,2-*a*]quinolines 6a−i and Indolizines 7a−c[a]



entry	substrate		product		yield[b]	entry	substrate		product		yield[b]
1		**4a**		**6a**	90	11		**4k**		**6k**	87
2		**4b**		**6b**	92	12		**4l**		**6l**	80
3		**4c**		**6c**	86	13		**4m**		**6m**	78[c]
4		**4d**		**6d**	88	14		**4n**		**6n**	75[c]
5		**4e**		**6e**	91	15		**4o**		**6o**	90
6		**4f**		**6f**	89	16		**4p**		**7a**	75
7		**4g**		**6g**	85	17		**4q**		**7b**	78
8		**4h**		**6h**	83	18		**4r**		**7c**	77
9		**4i**		**6i**	82	19		**4s**		**7d**	80
10		**4j**		**6j**	85	20		**3t**		**7e**	75

[a]Unless otherwise specified, all reactions were performed with alkynyl pyranoquinoline **4** (0.25 mmol), AgOTf (5.0 mol %) in 2.0 mL of CH_2Cl_2 at 25 °C for 3−4 h. [b]Isolated yields. [c]Reactions for 7−8 h.

the corresponding products **11** and **13** in 75 and 70% yields, respectively (Scheme 5).

■ COMPUTATIONAL STUDIES

In order to understand the site-selectivity for ring cyclization (Scheme 6) by C−C (path a) or N−C (path b) bond formation, quantum chemical calculations have been performed on the model system (**4d**; R^2 = Ph, R^3 = Ph).

The fate of this reaction depends on the prereaction complex (**PRC**; complex of **4** and $AgNO_3$), (Figure 2). In the formation of **PRC**, 11.73 kcal/mol [in complexation of reactants (**REC**) **4** and $AgNO_3$] energy is released. **PRC** may lead to two kinds of

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Scheme 3. Synthesis of 4-Iodopyrano[4,3-*b*]quinolines (2a–j) and 4-Alkynyl-pyrano[4,3-*b*]quinolines

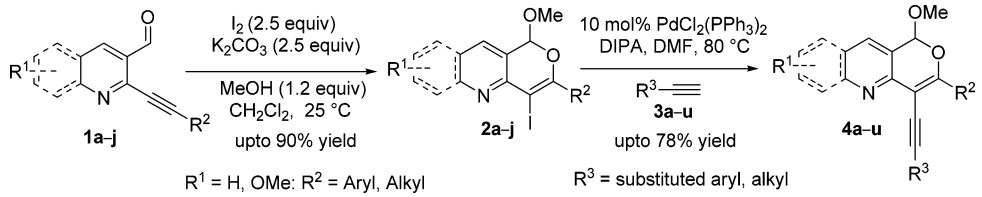
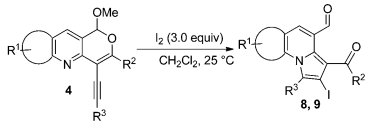


Table 3. Synthesis of Pyrrolo[1,2-*a*]quinolines 8a–j and Indolizines 9a–b[a]



entry	substrate	product	yield[b]	entry	substrate	product	yield[b]
1	**4a**	**8a**	81	7	**4u**	**8g**	77
2	**4b**	**8b**	84	8	**4j**	**8h**	75
3	**4d**	**8c**	80	9	**4n**	**8i**	70
4	**4f**	**8d**	82	10	**4o**	**8j**	80
5	**4g**	**8e**	78	11	**4q**	**9a**	70
6	**4h**	**8f**	75	12	**4s**	**9b**	72

[a]All reactions were performed with alkynyl pyranoquinoline **4** (0.25 mmol), I_2 (3.0 equiv) in 2.0 mL of CH_2Cl_2 at 25 °C for **3**–**4** h. [b]Isolated yields.

products, based on the attack of pyridine N (C–N bond formation) and/or phenyl CH (C–C bond formation). The 3D structures of **PRC**, transition states (**TS-1** and **TS-2**) and the intermediates (**INT-1** and **INT-2**) on the reaction paths a and b respectively were obtained using B3LYP optimization. In **PRC**, Ag metal is almost symmetrically attached to both alkynyl carbons (C1 and C2), but in the transition states, it is preferably attached to the C2 atom. Therefore, this C2 adapts sp^2 character, leading to an increased proximity between C1 and pyridine N or CH.

Figure 3 shows that the formation of **INT-2** is exothermic by 7.70 kcal/mol with an energy barrier of 9.01 kcal/mol. On the other hand, the energy barrier for the formation of **INT-1** is larger by 22.30 kcal/mol and leads to an endothermic **INT-1**. This establishes that the formation of a five membered ring through C–N bond formation is the preferred path as per thermodynamic as well as kinetic controls.

CONCLUSIONS

In summary, we have demonstrated the facile synthesis of substituted pyrrolo[1,2-*a*]quinolines and indolizines via electrophilic cyclization followed by ring-opening under mild reaction conditions using silver catalyst as well as inexpensive iodine. This chemistry involved the preferential nucleophilic attack of the pyridyl nitrogen over aryl ring onto the adjacent alkyne carbon to form *5-endo-dig* cyclized products. The formation of *5-endo-dig* cyclized products by the site-selective electrophilic cyclization was supported by the quantum chemical calculations between C–C (ΔE_a = 31.31 kcal/mol) and C–N (ΔE_a = 9.01 kcal/mol) bond of the substrate **4d**. The structure of the products were confirmed by the X-ray crystallographic studies. The cyclized products **8** and **9** embedded with iodo group could be a useful handle for further elaboration using palladium-catalyzed coupling reactions. From a synthetic

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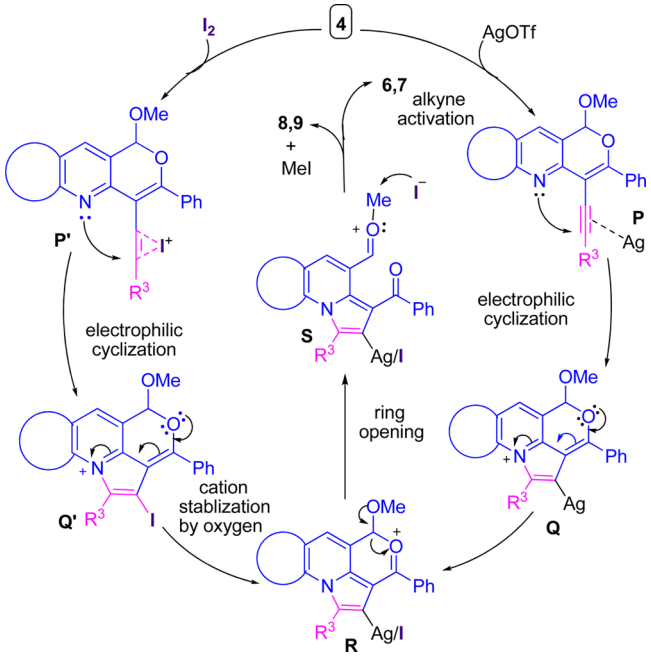
Scheme 4. Plausible Mechanism



point of view, the net transformation involves a one-step conversion of simple and readily available starting materials into an interesting class of heterocyclic compounds. This chemistry is expected to find application in organic synthesis in general and in the construction of a variety of compounds. Further investigations of this synthetic protocol are under progress and will be reported in due course.

EXPERIMENTAL PROCEDURES

General Method. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded in $CDCl_3$. Chemical shifts for carbons are reported in ppm from tetramethylsilane and are referenced to the carbon resonance of the solvent. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublet), coupling constants in Hertz, and integration. High-resolution mass spectra were recorded with electrospray mass spectrometer. Crystal structure analysis was accomplished on single crystal X-ray diffractometer. TLC analysis was performed on commercially prepared 60 F_{254} silica gel plates and visualized by either UV irradiation or by staining with I_2. All purchased chemicals were used as received.

The starting materials **2** were prepared by electrophilic iodocyclization using reported procedure.[15b,c] The structure and purity of known starting materials **2a,b**, **2d–g**,[15a,b] **2h** and **2j**[13e] were confirmed by comparison of their physical and spectral data (^{1}H NMR and ^{13}C NMR) with those reported in literature.

3-(4-Butylphenyl)-4-iodo-1-methoxy-1*H*-pyrano[4,3-*b*]-quinoline (2c). The product was obtained as light brown crystals (423.9 mg, 90% yield): mp 78–80 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (d, J = 8.0 Hz, 1H), 7.90 (s, 1H), 7.76 (d, J = 8.0 Hz, 1H), 7.66 (t, J = 8.8, 1H), 7.59 (d, J = 8.0 Hz, 2H), 7.43 (t, J = 7.6 Hz, 1H), 7.21–7.18 (m, 2H), 6.16 (s, 1H), 3.65 (s, 3H), 2.61 (t, J = 7.7 Hz, 2H), 1.60–1.54 (m, 2H), 1.35–1.29 (m, 2H), 0.88 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.8, 148.8, 148.0, 145.0, 134.1, 133.1, 130.2, 129.9, 129.4, 127.9, 127.5, 127.4, 126.3, 121.9, 100.4, 56.5, 35.6, 33.3, 22.4, 13.9; HRMS (ESI) calcd for $[C_{23}H_{22}INO_2]$ requires $[M]^+$ 471.0695, found $[M]^+$ 471.0698.

8-Iodo-5-methoxy-7-(*p*-tolyl)-5*H*-pyrano[4,3-*b*]pyridine (2i). The product was obtained as semisolid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 (d, J = 5.8 Hz, 1H), 7.60 (d, J = 8.0 Hz, 2H), 7.51(d, J = 7.3 Hz, 1H), 7.27 (s, 1H), 7.26–7.22 (m, 2H), 6.09 (s, 1H), 3.67 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.1, 150.7, 148.2, 139.9, 133.7, 133.3, 129.8, 128.6, 122.2, 99.9, 75.9, 56.1, 21.5; HRMS (ESI) calcd for $[C_{16}H_{14}INO_2]$ requires $[M]^+$ 379.0069, found $[M]^+$ 379.0070.

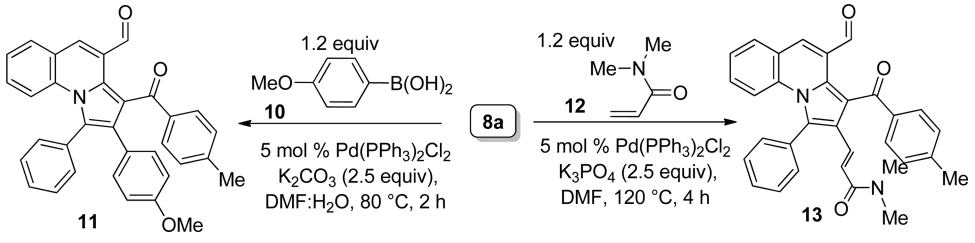
General Procedure for the Synthesis of Alkynyl-pyrano[4,3-*b*]quinoline and Pyridine 4a–u. To a solution of 4-iodopyranoquinoline **1** (0.25 mmol) in DMF were added 5 mol % of $PdCl_2(PPh_3)_2$. The reaction vial was then sealed and flushed with nitrogen. Then 3.0 equiv of DIPA and 1.2 equiv of alkyne were added. The reaction was then stirred at 80 °C until TLC revealed complete conversion of the starting material. The solution was allowed to cool and diluted with H_2O and then extracted with EtOAc. The combined organic layers were dried over Na_2SO_4, concentrated, and purified by column chromatography to afford the corresponding product. The structure and purity of known starting materials **4f,g**[15a] were confirmed by comparison of their physical and spectral data (^{1}H NMR and ^{13}C NMR) with those reported in literature.

1-Methoxy-4-(phenylethynyl)-3-(*p*-tolyl)-1*H*-pyrano[4,3-*b*]-quinoline (4a). The product was obtained as semisolid (151.2 mg, 75% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, J = 8.8 Hz, 1H), 8.11 (d, J = 8.0 Hz, 2H), 7.99 (s, 1H), 7.74 (d, J = 8.8 Hz, 1H), 7.65 (td, J = 1.4 and 6.6 Hz, 1H), 7.51 (dd, J = 1.4 and 8.0 Hz, 2H), 7.41 (t, J = 8.0 Hz, 1H), 7.29–7.21 (m, 5H), 6.25 (s, 1H), 3.68 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.5, 149.1, 149.0, 140.7, 132.9, 131.4, 131.3, 130.0, 129.0, 128.7, 128.2, 127.7, 127.6, 127.0, 126.0, 124.2, 122.0, 100.3, 95.7, 85.0, 56.4, 21.5; HRMS (ESI) calcd for $[C_{28}H_{21}NO_2]$ requires $[M]^+$ 403.1572, found $[M]^+$ 403.1575.

1-Methoxy-4-((4-methoxyphenyl)ethynyl)-3-(*p*-tolyl)-1*H*-pyrano[4,3-*b*]quinoline (4b). The product was obtained as a pale yellow solid (168.8 mg, 78%): mp 80–82 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24–8.18 (m, 3H), 8.06 (s, 1H), 7.81 (d, J = 8.0 Hz, 1H), 7.72 (t, J = 8.0 Hz, 1H), 7.53–7.49 (m, 3H), 7.29 (d, J = 8.0 Hz, 2H), 6.88 (d, J = 8.0 Hz, 2H), 6.32 (s, 1H), 3.83 (s, 3H), 3.75 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.4, 149.0, 140.7, 132.9, 131.4, 130.8, 130.0, 129.8, 129.0, 128.6, 127.6, 127.1, 126.0, 122.1, 116.5, 114.3, 113.8, 100.3, 95.9, 83.2, 56.4, 55.3, 21.6; HRMS (ESI) calcd for $[C_{29}H_{23}NO_3]$ requires $[M]^+$ 433.1678, found 433.1679.

1-Methoxy-4-(thiophen-3-ylethynyl)-3-(*p*-tolyl)-1*H*-pyrano-[4,3-*b*]quinoline (4c). The product was obtained as dark brown solid (149.2 mg, 73% yield): mp 100–102 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (d, J = 8.8 Hz, 1H), 8.17 (d, J = 8.0 Hz, 2H), 8.07 (s, 1H), 7.82 (d, J = 8.0 Hz, 1H), 7.72 (t, J = 6.6 Hz, 1H), 7.54–7.53 (m, 1H), 7.49 (t, J = 8.0 Hz, 1H), 7.30–7.28 (m, 3H), 7.26–7.24 (m, 1H), 6.31 (s, 1H), 3.74 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.3, 148.9, 140.9, 133.1, 131.1, 130.2, 129.9, 129.8, 129.6, 129.0,

Scheme 5. Pd-Catalyzed Cross-Coupling Reactions of 8a



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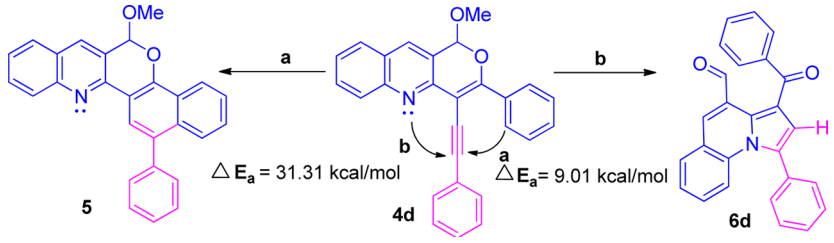
Scheme 6. Possible Site-Selective Electrophilic Cyclization



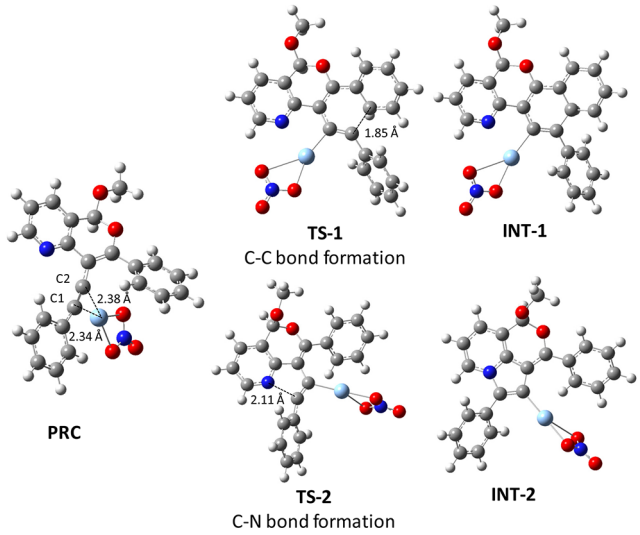


Figure 2. 3D geometry (B3LYP/6-31+G(d)) of **PRC**, transition states (**TS-1** and **TS-2**) and intermediates (**INT-1** and **INT-2**) (LanL2DZ basis set is used for Ag metal).

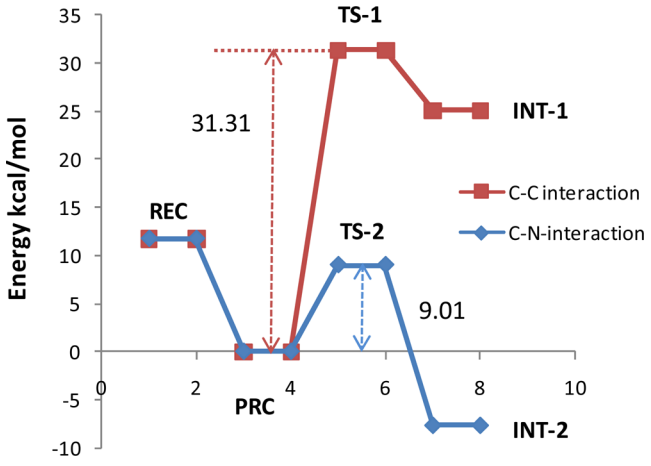


Figure 3. Potential energy surface for **PRC**, transition states (**TS-1** and **TS-2**) and intermediates (**INT-1** and **INT-2**) (B3LYP/6-31+(d)).

128.7, 128.1, 127.6, 127.0, 126.1, 124.9, 123.2, 122.6, 122.0, 100.3, 90.9, 84.0, 56.5, 21.6; HRMS (ESI) calcd for $[C_{26}H_{19}NO_2S]$ requires $[M]^+$ 409.1136, found $[M]^+$ 409.1140.

1-Methoxy-3-phenyl-4-(phenylethynyl)-1*H*-pyrano[4,3-*b*]-quinoline (4d). The product was obtained as semisolid (136.1 mg, 70% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21−8.16 (m, 3H), 8.00 (s, 1H), 7.75 (d, J = 8.0 Hz, 1H), 7.66 (td, J = 1.4 and 7.3 Hz, 1H), 7.48 (dd, J = 1.4 and 6.5 Hz, 2H), 7.43−7.41 (m, 4H), 7.29−7.23 (m, 3H), 6.27 (s, 1H), 3.69 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.0, 148.9, 148.7, 134.3, 132.9, 131.4, 130.3, 130.1, 129.9, 129.1, 128.2, 127.9, 127.8, 127.7, 126.2, 124.1, 121.9, 100.8, 100.5, 95.6, 84.7, 56.5; HRMS (ESI) calcd for $[C_{27}H_{19}NO_2]$ requires $[M]^+$ 389.1416, found $[M]^+$ 389.1422.

1-Methoxy-4-((4-methoxyphenyl)ethynyl)-3-phenyl-1*H*-pyrano[4,3-*b*]quinoline (4e). The product was obtained as semisolid (136.1 mg, 65% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22−8.16 (m, 3H), 8.02 (s, 1H), 7.76 (d, J = 8.0 Hz, 1H), 7.66 (td, J = 1.4 and 5.8 Hz, 1H), 7.45−7.40 (m, 6H), 6.80 (dd, J = 6.7 and 2.0 Hz, 2H), 6.27 (s, 1H), 3.76 (s, 3H), 3.69 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.3, 149.0, 134.3, 133.0, 132.9, 130.2, 130.1, 129.8, 129.0, 127.9, 127.6, 127.1, 126.1, 122.0, 116.3, 113.8, 101.0, 100.4, 95.9, 83.2, 56.4, 55.3; HRMS (ESI) calcd for $[C_{28}H_{21}NO_3]$ requires $[M]^+$ 419.1521, found $[M]^+$ 419.1522.

4-((4-Butylphenyl)ethynyl)-1-methoxy-3-phenyl-1*H*-pyrano-[4,3-*b*]quinoline (4h). The product was obtained as semisolid (151.3 mg, 68% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27−8.25 (m, 2H), 8.22 (d, J = 8.7 Hz, 1H), 8.06 (s, 1H), 7.80 (d, J = 8.2 Hz, 1H), 7.71 (td, J = 1.4 and 8.7 Hz, 1H), 7.50−7.45 (m, 6H), 7.14 (d, J = 8.0 Hz, 2H), 6.32 (s, 1H), 3.75 (s, 3H), 2.60 (t, J = 7.6 Hz, 2H), 1.59−1.57 (m, 2H), 1.39−1.33 (m, 2H), 0.92 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.5, 149.1, 149.0, 142.9, 134.2, 132.9, 131.3, 130.2, 130.0, 129.8, 129.0, 128.3, 127.9, 127.6, 127.1, 126.1, 122.0, 121.2, 101.1, 100.4, 96.0, 84.0, 56.4, 35.6, 33.4, 22.3, 13.9; HRMS (ESI) calcd for $[C_{31}H_{27}NO_2]$ requires $[M]^+$ 445.2042, found $[M]^+$ 445.2046.

3-(4-Butylphenyl)-1-methoxy-4-((4-methoxyphenyl)-ethynyl)-1*H*-pyrano[4,3-*b*]quinoline (4i). The product was obtained as semisolid (154.7 mg, 65% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24−8.20 (m, 3H), 8.03 (s, 1H), 7.78 (d, J = 8.0 Hz, 1H), 7.70 (t, J = 8.0 Hz, 1H), 7.52 (d, J = 8.8 Hz, 2H), 7.46 (t, J = 7.3 Hz, 1H), 7.29 (d, J = 8.8 Hz, 2H), 6.87 (d, J = 8.8 Hz, 2H), 6.28 (s, 1H), 3.80 (s, 3H), 3.72 (s, 3H) 2.68 (t, J = 7.32 Hz, 2H), 1.68−1.60 (m, 2H), 1.43−1.33 (m, 2H), 0.94 (t, J = 7.32 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.4, 149.2, 144.5, 132.9, 132.7, 131.5, 130.0, 129.7, 129.5, 129.0, 128.8, 128.1, 127.8, 127.6, 127.0, 126.0, 125.9, 122.0, 116.4, 113.9, 100.1, 95.7, 83.5, 56.4, 55.3, 35.6, 33.3, 22.3, 13.9; HRMS (ESI) calcd for $[C_{32}H_{29}NO_3]$ requires $[M + H]^+$ 476.2225, found $[M + H]^+$ 476.2225.

3-(4-Butylphenyl)-1-methoxy-4-(thiophen-3-ylethynyl)-1*H*-pyrano[4,3-*b*]quinoline (4j). The product was obtained as semisolid (139.8 mg, 62% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17−8.11 (m, 3H), 8.00 (s, 1H), 7.74 (d, J = 8.0 Hz, 1H), 7.65 (td, J = 1.4 and 5.8 Hz, 1H), 7.45 (d, J = 2.9 Hz, 1H), 7.41 (d, J = 7.3 Hz, 1H), 7.23−7.20 (m, 3H), 7.18 (s, 1H), 6.25 (s, 1H), 3.68 (s, 3H), 2.61 (t, J = 6.9 Hz, 2H), 1.59−1.56 (m, 2H), 1.34−1.26 (m, 2H), 0.89−0.85 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.0, 149.1, 149.0, 145.7, 133.0, 131.5, 130.1, 129.9, 129.7, 129.0, 128.0, 127.6, 127.0, 126.1, 124.9, 123.2, 122.0, 114.1, 100.3, 91.0, 84.2, 56.4, 35.6, 33.3, 22.4, 13.9; HRMS (ESI) calcd for $[C_{29}H_{25}NO_2S]$ requires $[M]^+$ 451.1606, found 451.1606.

3-(4-(*tert*-Butyl)phenyl)-1-methoxy-4-(*p*-tolylethynyl)-1*H*-pyrano[4,3-*b*]quinoline (4k). The product was obtained as semisolid (149.1 mg, 65% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34−8.30 (m, 3H), 8.08 (s, 1H), 7.83 (d, J = 8.0 Hz, 1H), 7.77 (t, J = 7.3 Hz, 1H), 7.59−7.56 (m, 4H), 7.52 (t, J = 6.7 Hz, 1H), 7.23 (d, J = 8.0 Hz, 2H), 6.35 (s, 1H), 3.79 (s, 3H), 2.42 (s, 3H), 1.44 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.5, 153.6, 149.1, 137.8, 132.9, 131.4, 131.2, 130.0, 129.7, 129.1, 128.9, 128.6, 127.6, 127.0, 125.0, 124.8, 122.8, 121.1, 100.2, 96.0, 84.3, 56.4, 34.9, 31.1, 21.5; HRMS (ESI)

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calcd for $[C_{32}H_{29}NO_2]$ requires $[M + H]^+$ 460.2276, found $[M + H]^+$ 460.2275.

3-(4-(*tert*-Butyl)phenyl)-4-((4-butylphenyl)ethynyl)-1-methoxy-1*H*-pyrano[4,3-*b*]quinoline (4l). The product was obtained as semisolid (162.8 mg, 65% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34−8.29 (m, 3H), 8.08 (s, 1H), 7.83 (d, J = 8.0 Hz, 1H), 7.76 (t, J = 8.0 Hz, 1H), 7.58−7.55 (m, 4H), 7.54−7.50 (m, 1H), 7.23 (d, J = 8.0 Hz, 2H), 6.34 (s, 1H), 3.78 (s, 3H), 2.67 (t, J = 7.3 Hz, 2H), 1.70−1.63 (m, 2H), 1.44−1.43 (m, 9H), 1.41−1.39 (m, 2H), 0.99 (t, J = 8.08 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.4, 153.6, 149.1, 142.8, 132.9, 131.4, 131.2, 130.0, 129.7, 128.8, 128.6, 128.4, 128.1, 127.6, 127.0, 125.9, 125.0, 122.0, 121.3, 100.1, 96.1, 84.3, 56.4, 35.6, 34.9, 33.3, 31.2, 22.3, 13.9; HRMS (ESI) calcd for $[C_{35}H_{35}NO_2]$ requires $[M + H]^+$ 502.2746, found $[M + H]^+$ 502.2746.

3-(4-Ethylphenyl)-1,8-dimethoxy-4-(phenylethynyl)-1*H*-pyrano[4,3-*b*]quinoline (4o). The product was obtained as a semisolid (167.6 mg, 75% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, J = 8.0 Hz, 2H), 8.06 (d, J = 8.8 Hz, 1H), 7.87 (s, 1H), 7.50 (d, J = 6.5 Hz, 2H), 7.32−7.22 (m, 6H), 7.00 (d, J = 2.2 Hz, 1H), 6.21 (s, 1H), 3.84 (s, 3H), 3.66 (s, 3H), 2.66 (q, J = 7.3 Hz, 2H), 1.21 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.2, 157.4, 146.8, 146.7, 144.7, 131.9, 131.4, 131.2, 130.3, 128.9, 128.0, 127.6, 127.3, 123.1, 122.9, 122.1, 105.3, 100.1, 99.6, 95.5, 84.6, 56.2, 55.3, 28.7, 15.1; HRMS (ESI) calcd for $[C_{30}H_{25}NO_3]$ requires $[M + H]^+$ 448.1912, found $[M + H]^+$ 448.1913.

5-Methoxy-7-phenyl-8-(*m*-tolylethynyl)-5*H*-pyrano[4,3-*b*]-pyridine (4p). The product was obtained as a semisolid (105.9 mg, 60% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.77 (d, J = 3.6 Hz, 1H), 8.22−8.20 (m, 2H), 7.59 (d, J = 5.8 Hz, 1H), 7.47−7.43 (m, 3H), 7.34−7.29 (m, 2H), 7.24 (t, J = 6.6 Hz, 1H), 7.17 (t, J = 8.0 Hz, 1H), 7.07 (d, J = 8.0 Hz, 1H), 6.19 (s, 1H), 3.67 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.5, 150.9, 148.8, 141.5, 137.7, 134.2, 133.5, 132.1, 130.1, 128.9, 128.7, 128.5, 128.0, 127.9, 125.0, 123.5, 122.0, 121.9, 99.9, 95.8, 84.0, 56.1, 21.2; HRMS (ESI) calcd for $[C_{24}H_{19}NO_2]$ requires $[M]^+$ 353.1416, found $[M]^+$ 353.1420.

5-Methoxy-8-(phenylethynyl)-7-*p*-tolyl-5*H*-pyrano[4,3-*b*]-pyridine (4q). The product was obtained as a semisolid (107.6 mg, 61% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.70 (d, J = 5.1 Hz, 1H), 8.07 (d, J = 8.0 Hz, 2H), 7.54−7.52 (m, 2H), 7.46−7.41 (m, 2H), 7.26−7.13 (m, 5H), 6.13 (s, 1H), 3.62 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.5, 151.1, 149.0, 140.4, 133.1, 131.4, 131.2, 128.8, 128.6, 128.4, 128.0, 127.98, 127.8, 127.7, 126.1, 124.0, 121.9, 121.6, 99.9, 99.4, 95.3, 84.8, 56.0, 21.3; HRMS (ESI) calcd for $[C_{24}H_{19}NO_2]$ requires $[M]^+$ 353.1416, found $[M]^+$ 353.1426.

5-Methoxy-7-(4-methoxyphenyl)-8-(phenylethynyl)-5*H*-pyrano[4,3-*b*]pyridine (4r). The product was obtained as a semisolid (116.2 mg, 63% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.69 (dd, J = 5.1 and 1.4 Hz, 1H), 8.15 (d, J = 8.8 Hz, 2H), 7.52 (dd, J = 7.3 and 1.4 Hz, 1H), 7.46 (dd, J = 8.0 and 1.4 Hz, 2H), 7.24−7.20 (m, 3H), 7.17−7.14 (m, 1H), 6.91 (d, J = 8.8 Hz, 2H), 6.12 (s, 1H), 3.81 (s, 3H), 3.62 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.2, 158.6, 151.0, 149.2, 133.2, 131.5, 130.7, 128.1, 127.7, 126.3, 122.0, 121.5, 113.3, 99.9, 98.5, 95.3, 84.9, 56.1, 55.4; HRMS (ESI) calcd for $[C_{24}H_{19}NO_3]$ requires $[M]^+$ 369.1365, found $[M]^+$ 369.1368.

5-Methoxy-7-(4-methoxyphenyl)-8-(*p*-tolylethynyl)-5*H*-pyrano[4,3-*b*]pyridine (4s). The product was obtained as a a semisolid (124.4 mg, 65% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.73 (dd, J = 2.2 and 5.1 Hz, 1H), 8.21 (dd, J = 2.2 and 6.5 Hz, 2H), 7.56 (dd, J = 1.4 and 7.3 Hz, 1H), 7.41 (d, J = 8.0 Hz, 2H), 7.20 (t, J = 5.1 Hz, 1H), 7.10 (d, J = 8.0 Hz, 2H), 6.96 (d, J = 8.7 Hz, 2H), 6.16 (s, 1H), 3.85 (s, 3H), 3.66 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.0, 158.0, 151.1, 149.3, 137.7, 133.1, 131.3, 130.6, 128.9, 126.6, 121.9, 121.4, 121.0, 113.3, 99.9, 98.8, 95.4, 84.2, 56.0, 55.3, 21.5; HRMS (ESI) calcd for $[C_{25}H_{21}NO_3]$ requires $[M]^+$ 383.1521, found $[M]^+$ 383.1524.

5-Methoxy-7-(4-methoxyphenyl)-8-(thiophen-3-ylethynyl)-5*H*-pyrano[4,3-*b*]pyridine (4t). The product was obtained as a semisolid (112.5 mg, 60% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.68 (dd, J = 1.4 and 5.1, 1H), 8.13 (dd, J = 2.2 and 6.6, 2H), 7.53−7.50 (m, 2H), 7.42 (d, J = 2.9 Hz, 1H), 7.19−7.12 (m, 2H), 6.91 (d, J = 8.7, 2H), 6.12 (s, 1H), 3.80 (s, 3H), 3.62 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.0, 158.2, 151.1, 149.1, 133.1, 130.5, 129.9, 129.4, 129.2, 128.0, 127.7, 126.5, 124.8, 123.0, 121.8, 121.5, 113.3, 99.9, 90.4, 84.2, 56.0, 55.3; HRMS (ESI) calcd for $[C_{22}H_{17}NO_3S]^+$ requires $[M]^+$ 375.0929, found 375.0923.

3-(4-Butylphenyl)-1-methoxy-4-(phenylethynyl)-1*H*-pyrano-[4,3-*b*]quinoline (4u). The product was obtained as a semisolid (160.2 mg, 72% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14−8.12 (m, 3H), 7.98 (s, 1H), 7.73 (d, J = 8.0 Hz, 1H), 7.65 (t, J = 8.0 Hz, 1H), 7.51 (d, J = 6.6 Hz, 2H), 7.41 (t, J = 8.0 Hz, 1H), 7.29−7.22 (m, 5H), 6.24 (s, 1H), 3.68 (s, 3H), 2.62 (d, J = 7.7 Hz, 2H), 1.60−1.56 (m, 2H), 1.34−1.29 (m, 2H), 0.87 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.2, 148.9, 148.6, 145.7, 133.2, 131.1, 130.2, 128.9, 128.0, 127.9, 127.62, 127.59, 126.9, 126.0, 123.9, 121.8, 100.0, 99.7, 95.5, 84.5, 56.3, 35.4, 33.2, 22.1, 13.7; HRMS (ESI) calcd for $[C_{31}H_{27}NO_2]^+$ requires $[M]^+$ 445.2042, found 445.2041.

General Procedure for the Synthesis of 3-Benzoyl-1-aryl Pyrrolo[1,2-*a*]quinoline-4-carbaldehyde 6a−o. To a vial 4-alkynl pyranoquinoline **3** (0.25 mmol) and 5 mol % AgOTf were added in DCM. The reaction vial was then sealed and stirred at room temperature until TLC revealed complete conversion of the starting material. The solution was diluted with H_2O and then extracted with EtOAc. The combined organic layers were dried over Na_2SO_4, concentrated, and purified by column chromatography to afford the corresponding product.

3-(4-Methylbenzoyl)-1-phenylpyrrolo[1,2-*a*]quinoline-4-carbaldehyde (6a). The product was obtained as a yellow solid (87.5 mg, 90% yield): mp 150−152 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.26 (s, 1H), 7.94−7.89 (m, 3H), 7.86 (dd, J = 1.4 and 6.6 Hz, 1H), 7.52−7.48 (m, 6H), 7.39 (td, J = 0.7 and 6.5 Hz, 1H), 7.32−7.28 (m, 3H), 6.97 (s, 1H), 2.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.7, 188.9, 143.0, 136.6, 134.7, 134.2, 131.0, 130.8, 130.0, 129.8, 129.4, 129.0, 128.9, 128.6, 128.2, 128.1, 125.0, 124.2, 120.3, 118.3, 116.8, 21.6; HRMS (ESI) calcd for $[C_{27}H_{19}NO_2]$ requires $[M]^+$ 389.1416, found $[M]^+$ 389.1416.

1-(4-Methoxyphenyl)-3-(4-methylbenzoyl)pyrrolo[1,2-*a*]-quinoline-4-carbaldehyde (6b). The product was obtained as yellow crystals (96.3 mg, 92% yield): mp 164−166 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.18 (s,1H), 7.83 (d, J = 8.0 Hz, 3H), 7.77 (dd, J = 5.8 and 1.4 Hz, 1H), 7.49 (d, J = 8.7 Hz, 1H), 7.33−7.29 (m, 3H), 7.25 (dd, J = 8.8 and 1.4 Hz, 1H), 7.24−7.20 (m, 2H), 6.94 (d, J = 8.8 Hz, 2H), 6.86 (s, 1H), 3.83 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.7, 189.0, 160.0, 142.9, 140.7, 136.7, 135.1, 132.9, 130.8, 130.0, 129.8, 128.6, 127.9, 127.6, 126.3, 126.0, 124.9, 122.0, 120.0, 118.0, 116.5, 114.3, 100.3, 55.4, 21.6; HRMS (ESI) calcd for $[C_{28}H_{21}NO_3]$ requires $[M]^+$ 419.1521, found $[M]^+$ 419.1520.

3-(4-Methylbenzoyl)-1-(thiophen-3-yl)pyrrolo[1,2-*a*]-quinoline-4-carbaldehyde (6c). The product was obtained as yellow crystals (84.9 mg, 86% yield): mp 180−182 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.25 (s, 1H), 7.93 (s, 1H), 7.90−7.85 (m, 3H), 7.57 (d, J = 8.0 Hz, 1H), 7.50−7.48 (m, 2H), 7.41−7.37 (m, 2H), 7.29 (d, J = 8.0 Hz, 2H), 7.12 (dd, J = 5.1 and 1.4 Hz, 1H), 7.00 (s, 1H), 2.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.4, 188.9, 143.4, 136.8, 135.1, 134.2, 131.0, 130.8, 130.3, 129.8, 129.0, 128.8, 128.1, 126.6, 125.6, 125.1, 125.0, 124.2, 120.5, 117.6, 116.6, 21.6; HRMS (ESI) calcd for $[C_{25}H_{17}NO_2S]$ requires $[M]^+$ 395.0980, found $[M]^+$ 395.0985.

3-Benzoyl-1-phenylpyrrolo[1,2-*a*]quinoline-4-carbaldehyde (6d). The product was obtained as a yellow solid (82.5 mg, 88% yield): mp 150−152 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.23 (s, 1H), 7.93−7.89 (m, 3H), 7.80 (d, J = 7.3 Hz, 1H), 7.50 (t, J = 7.3 Hz, 1H), 7.45−7.40 (m, 8H), 7.32 (t, J = 6.6 Hz, 1H), 7.24 (td, J = 1.4 and 8.8 Hz, 1H), 6.90 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.8, 188.9, 139.3, 134.8, 134.1, 132.2, 131.1, 130.8, 130.1, 129.6, 129.4, 128.9, 128.7, 128.3, 128.2, 125.0, 124.3, 120.4, 118.3, 116.6. HRMS (ESI) calcd for $[C_{26}H_{17}NO_2]$ requires $[M]^+$ 375.1259, found $[M]^+$ 375.1261.

3-Benzoyl-1-(4-methoxyphenyl)pyrrolo[1,2-*a*]quinoline-4-carbaldehyde (6e). The product was obtained as a yellow solid (92.1 mg, 91% yield): mp 160−162 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ

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10.22 (s, 1H), 7.92 (d, J = 7.3 Hz, 2H), 7.86 (s, 1H), 7.80 (dd, J = 1.4 and 7.3 Hz, 1H), 7.52−7.48 (m, 2H), 7.44−7.40 (m, 2H), 7.34−7.30 (m, 3H), 7.26 (dd, J = 1.8 and 8.7 Hz, 1H), 6.94 (dd, J = 2.2 and 6.6 Hz, 2H), 6.86 (s, 1H), 3.83 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.8, 189.0, 159.9, 139.4, 135.0, 132.1, 131.0, 130.9, 130.8, 130.1, 129.6, 128.3, 128.2, 128.1, 126.4, 125.0, 124.3, 120.1, 118.1, 116.4, 114.3, 55.4; HRMS (ESI) calcd for $[C_{27}H_{19}NO_3]$ requires $[M]^+$ 405.1365, found $[M]^+$ 405.1366.

3-Benzoyl-1-(*p*-tolyl)pyrrolo[1,2-*a*]quinoline-4-carbaldehyde (6f). The product was obtained as yellow crystals (86.5 mg, 89% yield): mp 130−132 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.3 (s, 1H), 7.98 (d, J = 7.3 Hz, 2H), 7.94 (m, 1H), 7.87 (d, J = 7.3 Hz, 1H), 7.58−7.56 (m, 2H), 7.50−7.47 (m, 2H), 7.41−7.34 (m, 3H), 7.32−7.28 (m, 3H), 6.94 (s, 1H), 2.46 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.8, 188.9, 139.3, 138.7, 134.9, 132.1, 131.2, 130.8, 130.0, 129.6, 129.4, 129.3, 128.2, 125.0, 124.9, 124.3, 120.3, 120.2, 118.1, 116.5, 21.5; HRMS (ESI) calcd for $[C_{27}H_{19}NO_2]$ requires $[M]^+$ 389.1416, found $[M]^+$ 389.1417.

3-Benzoyl-1-(thiophen-3-yl)pyrrolo[1,2-*a*]quinoline-4-carbaldehyde (6g). The product was obtained as a orange solid (80.9 mg, 85% yield): mp 168−170 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.21 (s, 1H), 7.92−7.88 (m, 3H), 7.80 (dd, J = 1.4 and 7.3 Hz, 1H), 7.52−7.48 (m, 2H), 7.44−7.40 (m, 4H), 7.37−7.29 (m, 2H), 7.60 (dd, J = 1.4 and 4.4 Hz, 1H), 6.93 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.6, 188.9, 139.3, 135.0, 134.1, 132.2, 130.8, 130.4, 129.6, 128.8, 128.3, 128.1, 126.6, 125.7, 125.1, 125.0, 124.2, 120.6, 117.6, 116.3; HRMS (ESI) calcd for $[C_{24}H_{15}NO_2S]$ requires $[M]^+$ 381.0823, found $[M]^+$ 381.0825.

3-Benzoyl-1-(4-butylphenyl)pyrrolo[1,2-*a*]quinoline-4-carbaldehyde (6h). The product was obtained as a yellow solid (89.4 mg, 83% yield): mp 140−142 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.22 (s, 1H), 7.90 (dd, J = 2.2 and 6.6 Hz, 2H), 7.86 (s, 1H), 7.78 (dd, J = 1.4 and 7.3 Hz, 1H), 7.50−7.45 (m, 2H), 7.40 (t, J = 8.0 Hz, 2H), 7.32−7.29 (m, 3H), 7.24−7.20 (m, 3H), 6.87 (s, 1H), 2.63 (t, J = 8.0 Hz, 2H), 1.64−1.54 (m, 2H), 1.36−1.31 (m, 2H), 0.89 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.8, 189.0, 143.7, 139.4, 134.9, 132.1, 131.3, 131.2, 130.8, 130.0, 129.6, 129.3, 128.9, 128.3, 128.2, 128.1, 125.0, 124.3, 118.2, 116.4, 35.5, 33.5, 22.3, 13.9; HRMS (ESI) calcd for $[C_{30}H_{25}NO_2]$ requires $[M]^+$ 431.1885, found $[M]^+$ 431.1892.

3-(4-Butylbenzoyl)-1-(4-methoxyphenyl)pyrrolo[1,2-*a*]quinoline-4-carbaldehyde (6i). The product was obtained as yellow crystals (94.5 mg, 82% yield): mp 170−172 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.27 (s, 1H), 7.93−7.91 (m, 3H), 7.85 (d, J = 7.3 Hz, 1H), 7.56 (d, J = 8.7 Hz, 1H), 7.41−7.36 (m, 3H), 7.33−7.28 (m, 3H), 7.01 (d, J = 8.7 Hz, 2H), 6.94 (s, 1H), 3.90 (s, 3H), 2.68 (t, J = 7.6 Hz, 2H), 1.65−1.62 (m, 2H), 1.40−1.33 (m, 2H), 0.94 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.7, 189.0, 159.9, 147.9, 136.8, 135.0, 130.9, 130.0, 129.8, 128.4, 128.2, 127.8, 126.5, 124.9, 124.3, 120.1, 118.0, 116.6, 114.3, 55.4, 35.7, 33.3, 22.3, 13.9; HRMS (ESI) calcd for $[C_{31}H_{27}NO_3]$ requires $[M]^+$ 461.1991, found $[M]^+$ 461.1992.

3-(4-Butylbenzoyl)-1-(thiophen-3-yl)pyrrolo[1,2-*a*]quinoline-4-carbaldehyde (6j). The product was obtained as a yellow solid (92.8 mg, 85% yield): mp 106−108 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.26 (s, 1H), 7.94−790 (m, 3H), 7.87 (dd, J = 2.2 and 8.0 Hz, 1H), 7.58 (d, J = 6.6 Hz, 1H), 7.50−7.48 (m, 2H), 7.43−7.37 (m, 2H), 7.30 (d, J = 8.0 Hz, 2H), 7.13 (dd, J = 3.6 and 5.1 Hz, 1H), 7.01 (s, 1H), 2.69 (t, J = 7.3 Hz, 2H), 1.68−1.60 (m, 2H), 1.42−1.37 (m, 2H), 0.94 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.7, 188.9, 148.0, 136.9, 135.0, 134.2, 131.1, 130.8, 130.3, 129.8, 128.8, 128.4, 128.1, 128.0, 126.6, 125.6, 125.0, 124.2, 120.5, 117.6, 116.4, 35.7, 33.3, 22.3, 13.9; HRMS (ESI) calcd for $[C_{28}H_{23}NO_2S]$ requires $[M]^+$ 437.1449, found 437.1450.

3-(4-(*tert*-Butyl)benzoyl)-1-(*p*-tolyl)pyrrolo[1,2-*a*]quinoline-4-carbaldehyde (6k). The product was obtained as a yellow solid (96.7 mg, 87% yield): mp 180−182 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.22 (s, 1H), 7.89−7.86 (m, 3H), 7.79 (d, J = 8.0 Hz, 1H), 7.49 (d, J = 8.0 Hz, 1H), 7.43 (d, J = 8.0 Hz, 2H), 7.33−7.29 (m, 3H), 7.26−7.20 (m, 3H), 6.89 (s, 1H), 2.39 (s, 3H), 1.29 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.6, 189.1, 155.9, 138.6, 136.5, 134.8, 131.3, 131.1, 130.8, 129.9, 129.7, 129.6, 129.3, 128.3, 127.8, 125.3, 124.9, 124.2, 120.3, 118.2, 116.7, 35.1, 31.1, 21.4; HRMS (ESI) calcd for $[C_{31}H_{27}NO_2]$ requires $[M]^+$ 445.2042, found $[M]^+$ 445.2043.

3-(4-(*tert*-Butyl)benzoyl)-1-(4-butylphenyl)pyrrolo[1,2-*a*]quinoline-4-carbaldehyde (6l). The product was obtained as yellow solid (97.4 mg, 80% yield): mp 158−160 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.27 (s, 1H), 7.94−7.91 (m, 3H), 7.84 (d, J = 8.7 Hz, 1H), 7.52 (d, J = 9.5 Hz, 1H), 7.48 (d, J = 8.0 Hz, 2H), 7.37−7.34 (m, 3H), 7.30−7.25 (m, 3H), 6.95 (s, 1H), 2.67−2.69 (m, 2H), 169−1.62 (m, 2H), 1.42−1.34 (m, 2H), 1.32 (s, 9H), 0.95 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.6, 189.0, 155.9, 143.6, 136.5, 134.9, 131.4, 131.1, 130.8, 129.9, 129.7, 129.4, 128.9, 128.3, 127.8, 125.3, 124.9, 124.3, 120.3, 118.2, 116.6, 35.5, 35.1, 33.4, 31.2, 22.4, 14.0; HRMS (ESI) calcd for $[C_{34}H_{33}NO_2]$ requires $[M + H]^+$ 488.2589, found $[M + H]^+$ 488.2589.

3-Pentanoyl-1-phenylpyrrolo[1,2-*a*]quinoline-4-carbaldehyde (6m). The product was obtained as a brown solid (69.2 mg, 78% yield): mp 128−130 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.36 (s, 1H), 7.81 (s, 1H), 7.76 (dd, J = 1.4 and 8.0 Hz, 1H), 7.49−7.36 (m, 6H), 7.30 (t, J = 7.3 Hz, 1H), 7.21 (dd, J = 1.4 and 7.3 Hz, 1H), 7.05 (s, 1H), 2.88 (t, J = 5.2 Hz, 2H), 1.72−1.69 (m, 2H), 1.39−1.33 (m, 2H), 0.89 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.2, 189.5, 134.4, 134.3, 131.5, 130.7, 129.8, 129.4, 129.1, 128.9, 128.7, 127.4, 125.0, 124.3, 118.3, 118.2, 116.9, 40.5, 27.0, 22.6, 14.1; HRMS (ESI) calcd for $[C_{24}H_{21}NO_2]$ requires $[M + H]^+$ 356.1650, found $[M + H]^+$ 356.1650.

3-(Cyclohexanecarbonyl)-1-phenylpyrrolo[1,2-*a*]quinoline-4-carbaldehyde (6n). The product was obtained as a pale yellow solid (71.4 mg, 75% yield): mp 118−120 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.3 (s, 1H), 7.79 (s, 1H), 7.75 (dd, J = 1.4 and 7.3 Hz, 1H), 7.42 (s, 5H), 7.39 (d, J = 8.8 Hz, 1H), 7.29 (t, J = 8.0 Hz, 1H), 7.22−7.18 (m, 1H), 7.04 (s, 1H), 3.11−3.05 (m, 1H), 1.91−1.88 (m, 2H), 1.81−1.77 (m, 2H), 1.67−1.64 (m, 1H), 1.54−1.50 (m, 2H), 1.34−1.25 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.5, 189.2, 134.4, 134.3, 131.5, 131.1, 130.7, 129.7, 129.4, 129.1, 128.9, 128.7, 127.3, 125.0, 124.3, 118.1, 118.0, 116.1, 45.0, 29.7, 29.5, 25.9; HRMS (ESI) calcd for $[C_{26}H_{23}NO_2]$ requires $[M]^+$ 381.1729, found $[M]^+$ 381.1731.

3-(4-Ethylbenzoyl)-7-methoxy-1-phenylpyrrolo[1,2-*a*]quinoline-4-carbaldehyde (6o). The product was obtained as orange crystals (97.4 mg, 90% yield): mp 178−180 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.31 (s, 1H), 7.92 (d, J = 8.0 Hz, 2H), 7.88 (s, 1H), 7.46 (s, 6H), 7.41 (d, J = 9.5 Hz, 1H), 7.30 (d, J = 8.0 Hz, 2H), 6.94 (s, 1H), 6.89 (dd, J = 2.9 and 9.5 Hz, 1H), 3.87 (s, 3H), 2.72 (q, J = 7.3 Hz, 2H), 1.27 (t, J = 8.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.3, 189.1, 156.3, 149.0, 136.9, 134.2, 131.0, 130.5, 129.9, 129.4, 129.2, 128.8, 128.6, 127.8, 127.4, 125.6, 120.3, 119.6, 119.0, 116.4, 111.3, 55.6, 28.9, 15.3; HRMS (ESI) calcd for $[C_{29}H_{23}NO_3]$ requires $[M]^+$ 433.1678, found $[M]^+$ 433.1680.

General Procedure for the Synthesis of 1-Benzoyl-3-arylindolizine-8-carbaldehyde 7a−e. To a vial 4-alkynl pyranoquinoline **3** (0.25 mmol) and 5 mol % AgOTf were added in DCM. The reaction was then sealed and stirred at room temperature until TLC revealed complete conversion of the starting material. The solution was diluted with H_2O and then extracted with EtOAc. The combined organic layers were dried over Na_2SO_4, concentrated, and purified by column chromatography to afford the corresponding product.

1-Benzoyl-3-(*m*-tolyl)indolizine-8-carbaldehyde (7a). The product was obtained as a yellow solid (63.5 mg, 75% yield): mp 100−102 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.57 (s, 1H), 8.40 (d, J = 7.3 Hz, 1H), 7.86 (d, J = 8.0 Hz, 2H), 7.66 (d, J = 7.3 Hz, 1H), 7.50−7.46 (m, 1H), 7.43−7.39 (m, 2H), 7.32 (t, J = 8.0 Hz, 1H), 7.24−7.23 (m, 2H), 7.18 (t, J = 4.4 Hz, 1H), 6.84 (t, J = 7.3 Hz, 1H), 7.05 (s, 1H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.0, 190.0, 139.9, 139.2, 133.1, 131.7, 130.1, 129.7, 129.6, 129.4, 129.2, 128.2, 127.6, 127.5, 125.9, 119.8, 119.7, 114.0, 112.8, 112.7, 21.4; HRMS (ESI) calcd for $[C_{23}H_{17}NO_2]$ requires $[M + H]^+$ 340.1337, found $[M + H]^+$ 340.1337.

1-(4-Methylbenzoyl)-3-phenylindolizine-8-carbaldehyde (7b). The product was obtained as a brown solid (66.1 mg, 78% yield): mp 140−142 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.53 (s,

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1H), 8.39 (dd, J = 1.4 and 6.6 Hz, 1H), 7.79 (d, J = 8.0 Hz, 2H), 7.65 (dd, J = 1.4 and 6.6 Hz, 1H), 7.46−7.45 (m, 4H), 7.40−7.38 (m, 1H), 7.22 (d, J = 8.0 Hz, 2H), 7.09 (s, 1H), 6.83 (t, J = 6.6 Hz, 1H), 2.37 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.0, 190.0, 142.6, 137.1, 132.8, 130.4, 129.7, 129.3, 129.0, 128.7, 127.4, 125.7, 119.7, 114.0, 112.7, 21.6; HRMS (ESI) calcd for $[C_{23}H_{17}NO_2]$ requires $[M]^+$ 339.1259, found $[M]^+$ 339.1260.

1-(4-Methoxybenzoyl)-3-phenylindolizine-8-carbaldehyde (7c). The product was obtained as a orange solid (67.4 mg, 76% yield): mp 110−112 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.46 (s, 1H), 8.38 (d, J = 6.6 Hz, 1H), 790−7.88 (m, 2H), 7.62 (d, J = 6.6 Hz, 1H), 7.45−7.44 (m, 4H), 7.38−7.35 (m, 1H), 7.09 (s, 1H), 6.90 (d, J = 8.8 Hz, 2H), 6.81 (t, J = 7.3 Hz, 1H), 3.81 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.1, 189.8, 162.7, 139.2, 132.7, 132.3, 131.8, 130.4, 129.3, 129.0, 128.9, 128.7, 127.4, 127.0, 125.6, 119.4, 114.3, 114.0, 113.5, 112.5, 55.4; HRMS (ESI) calcd for $[C_{23}H_{17}NO_3]$ requires $[M]^+$ 355.1208, found $[M]^+$ 355.1209.

1-(4-Methoxybenzoyl)-3-*p*-tolylindolizine-8-carbaldehyde (7d). The product was obtained as yellow solid (73.8 mg, 80% yield): mp 130−132 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.48 (s, 1H), 8.36 (d, J = 5.8 Hz, 1H), 7.88 (dd, J = 2.2 and 6.6 Hz, 2H), 7.61 (dd, J = 1.4 and 5.8 Hz, 1H), 7.34 (d, J = 8.0 Hz, 2H), 7.25 (d, J = 8.0 Hz, 2H), 7.06 (s, 1H), 6.90 (dd, J = 2.2 and 6.6 Hz, 2H), 6.80 (t, J = 7.3 Hz, 1H), 3.81 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.1, 189.9, 162.7, 138.8, 132.6, 132.4, 132.0, 131.8, 129.9, 129.0, 128.9, 128.4, 127.4, 125.4, 119.2, 114.2, 113.5, 112.4, 55.5, 21.3; HRMS (ESI) calcd for $[C_{24}H_{19}NO_3]$ requires $[M]^+$ 369.1365, found $[M]^+$ 369.1366.

1-(4-Methoxybenzoyl)-3-(thiophen-3-yl)indolizine-8-carbaldehyde (7e). The product was obtained as brown solid (63.1 mg, 75% yield): mp 160−162 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.47 (s, 1H), 8.38 (d, J = 5.8 Hz, 1H), 7.89 (dd, J = 2.2 and 6.6 Hz, 2H), 7.63 (d, J = 8.0 Hz, 1H), 7.47−7.45 (m, 1H), 7.43−7.42 (m, 1H), 7.22 (dd, J = 1.4 and 5.1 Hz, 1H), 7.11 (s, 1H), 6.92 (d, J = 9.5 Hz, 2H), 6.85 (t, J = 7.3 Hz, 1H), 3.82 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.1, 189.8, 162.7, 132.6, 132.4, 131.8, 130.7, 129.0, 127.5, 125.5, 124.0, 122.3, 119.5, 114.1, 113.6, 112.6, 55.5; HRMS (ESI) calcd for $[C_{21}H_{15}NO_3S]$ requires $[M]^+$ 361.0773, found 361.0774.

General Procedure for the Synthesis of 3-Benzoyl-2-iodo-1-aryl-pyrrolo[1,2-*a*]quinoline-4-carbaldehyde 8a−j. To a vial 4-alkynl pyranoquinoline **3** (0.25 mmol) and 3.0 equiv of I_2 were added in DCM. The reaction vial was then sealed and stirred at room temperature until TLC revealed complete conversion of the starting material. The solution was washed with saturated solution of $Na_2S_2O_3$ and then extracted with EtOAc. The combined organic layers were dried over Na_2SO_4, concentrated, and purified by column chromatography to afford the corresponding product.

2-Iodo-3-(4-methylbenzoyl)-1-phenylpyrrolo[1,2-a]-quinoline-4-carbaldehyde (8a). The product was obtained as a brown solid (104.2 mg, 81% yield): mp 160−162 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.79 (s, 1H), 7.84 (d, J = 8.0 Hz, 2H), 7.78 (d, J = 7.3 Hz, 1H), 7.72 (s, 1H), 7.56−7.54 (m, 3H), 7.44−7.42 (m, 2H), 7.34−7.30 (m, 1H), 7.25−7.24 (m, 3H), 7.21−7.19 (m, 1H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.2, 188.0, 143.8, 136.0, 135.0, 134.4, 132.4, 132.2, 131.2, 131.0, 130.8, 130.5, 130.2, 129.4, 129.3, 128.8, 127.8, 126.1, 125.7, 124.9, 123.0, 121.3, 117.9, 21.8; HRMS (ESI) calcd for $[C_{27}H_{18}INO_2]$ requires $[M]^+$ 515.0382, found $[M]^+$ 515.0382.

2-Iodo-1-(4-methoxyphenyl)-3-(4-methylbenzoyl)pyrrolo-[1,2-a]quinoline-4-carbaldehyde (8b). The product was obtained as brown crystals (114.4 mg, 845 yield): mp 178−180 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.78 (s, 1H), 7.84 (d, J = 8.0 Hz, 2H), 7.77 (d, J = 8.0 Hz, 1H), 7.70 (s, 1H), 7.35−7.33 (m, 3H), 7.31−7.28 (m, 3H), 7.25 (s, 1H), 7.07 (d, J = 8.8 Hz, 2H), 3.92 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.3, 188.0, 160.3, 143.8, 136.0, 135.1, 132.4, 132.3, 132.1, 131.0, 130.7, 130.2, 129.3, 126.4, 126.1, 125.5, 124.8, 123.0, 121.1, 117.8, 114.7, 55.3, 21.8; HRMS (ESI) calcd for $[C_{28}H_{20}INO_3]$ requires $[M]^+$ 545.0488, found $[M]^+$ 545.0489.

3-Benzoyl-2-iodo-1-phenylpyrrolo[1,2-*a*]quinoline-4-carbaldehyde (8c). The product was obtained as a dark yellow solid (100.2 mg, 80% yield): mp 154−156 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.73 (s, 1H), 7.90 (d, J = 7.3 Hz, 2H), 7.73 (d, J = 7.3 Hz, 1H), 7.68 (s, 1H), 7.51−7.47 (m, 4H), 7.41−7.37 (m, 4H), 7.28 (t, J = 7.2 Hz, 1H), 7.20−7.15 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.5, 187.9, 138.5, 135.0, 134.4, 132.9, 132.6, 132.5, 131.2, 131.0, 130.8, 130.0, 129.5, 129.3, 128.5, 126.1, 125.7, 124.9, 123.0, 121.2, 118.0; HRMS (ESI) calcd for $[C_{26}H_{16}INO_2]$ requires $[M + H]^+$ 502.0304, found $[M + H]^+$ 502.0305.

3-Benzoyl-2-iodo-1-*p*-tolylpyrrolo[1,2-*a*]quinoline-4-carbaldehyde (8d). The product was obtained as a brown solid (105.5 mg, 82% yield): mp 168−170 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.80 (s, 1H), 7.96 (d, J = 8.0 Hz, 2H), 7.80 (d, J = 7.3 Hz, 1H), 7.74 (s,1H), 7.57 (t, J = 7.0 Hz, 1H), 7.48−7.45 (m, 2H), 7.39−7.37 (m, 2H), 7.34−7.29 (m, 5H), 2.51 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.7, 187.1, 138.6, 137.6, 134.1, 131.9, 131.6, 130.4, 130.0, 129.8, 129.1, 127.6, 125.2, 124.6, 123.9, 122.0, 120.1, 117.1, 20.7; HRMS (ESI) calcd for $[C_{27}H_{18}INO_2]$ requires $[M]^+$ 515.0382, found $[M]^+$ 515.0341.

3-Benzoyl-2-iodo-1-(thiophen-3-yl)pyrrolo[1,2-*a*]quinoline-4-carbaldehyde (8e). The product was obtained as a dark yellow solid (98.6 mg, 78% yield): mp 160−162 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.72 (s, 1H), 7.89 (dd, J = 1.4 and 8.0 Hz, 2H), 7.75−7.73 (m, 1H), 7.68 (s, 1H), 7.53−7.49 (m, 2H), 7.48−7.46 (m, 1H), 7.39 (d, J = 8.0 Hz, 2H), 7.33−7.29 (m, 2H), 7.28−7.24 (m, 1H), 7.06 (dd, J = 1.6 and 5.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.4, 187.9, 138.5, 135.1, 133.8, 132.9, 132.7, 131.3, 130.7, 130.0, 129.2, 128.5, 127.8, 127.1, 126.0, 125.8, 125.0, 123.0, 121.1, 117.5; HRMS (ESI) calcd for $[C_{24}H_{14}INO_2S]$ requires $[M]^+$ 506.9790, found 506.9793.

3-Benzoyl-1-(4-butylphenyl)-2-iodopyrrolo[1,2-*a*]quinoline-4-carbaldehyde (8f). The product was obtained as a dark yellow solid (104.4 mg, 75% yield): mp 158−160 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.79 (s, 1H), 7.96 (d, J = 7.3 Hz, 2H), 7.79 (d, J = 8.0 Hz, 1H), 7.73 (s, 1H), 7.56 (t, J = 8.0 Hz, 1H), 7.46 (t, J = 6.4 Hz, 2H), 7.39−7.33 (m, 5H), 7.25 (s, 2H), 2.76 (t, J = 8.8 Hz, 2H), 1.77−1.69 (m, 2H), 1.46−1.41 (m, 2H), 0.99 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.8, 188.0, 144.5, 138.5, 135.1, 132.9, 132.4, 131.5, 131.6, 131.0, 130.7, 130.1, 129.3, 128.5, 126.1, 125.6, 124.8, 123.0, 121.1, 118.0, 35.6, 33.3, 22.4, 14.0; HRMS (ESI) calcd for $[C_{30}H_{24}INO_2]$ requires $[M]^+$ 557.0852, found $[M]^+$ 557.0859.

3-(4-Butylbenzoyl)-2-iodo-1-phenylpyrrolo[1,2-*a*]quinoline-4-carbaldehyde (8g). The product was obtained as a yellow solid (107.2 mg, 77% yield): mp 170−172 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.78 (s, 1H), 7.85 (d, J = 8.0 Hz, 2H), 7.77 (d, J = 7.3 Hz, 1H), 7.72 (s, 1H), 7.56−7.55 (m, 3H), 7.44−7.42 (m, 2H), 7.32 (t, J = 6.6 Hz, 1H), 7.27−7.21 (m, 4H), 2.65(t, J = 7.6 Hz, 2H), 1.65−1.57 (m, 2H), 1.38−1.32 (m, 2H), 0.91 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.3, 187.9, 148.7, 136.2, 135.0, 134.4, 132.4, 131.9, 131.2, 130.9, 130.8, 130.2, 129.5, 129.3, 128.6, 126.2, 125.8, 124.9, 123.0, 121.3, 118.6, 35.8, 33.1, 22.4, 13.9; HRMS (ESI) calcd for $[C_{30}H_{24}INO_2]^+$ requires m/z 557.0852, found 557.0853.

3-(4-Butylbenzoyl)-2-iodo-1-(thiophen-3-yl)pyrrolo[1,2-*a*]-quinoline-4-carbaldehyde (8h). The product was obtained as a brown solid (105.5 mg, 75% yield): mp 210−212 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.99 (s, 1H), 8.10 (s, 1H), 7.87 (d, J = 8.0 Hz, 2H), 7.60−7.54 (m, 2H), 7.38 (d, J = 8.8 Hz, 1H), 7.35 (s, 1H), 7.23−7.21 (m, 2H), 7.18 (s, 3H), 2.60 (t, J = 7.3 Hz, 2H), 1.56−1.54 (m, 2H), 1.34−1.28 (m, 2H), 0.89−0.80 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.5, 186.0, 150.5, 147.9, 146.4, 140.2, 137.2, 136.7, 134.7, 130.1, 129.5, 128.7, 128.6, 128.5, 127.2, 127.1, 126.2, 123.9, 121.3, 118.2, 35.6, 33.4, 22.3, 13.9; HRMS (ESI) calcd for $[C_{28}H_{22}INO_2S]$ requires $[M]^+$ 563.0416, found $[M]^+$ 563.0416.

3-(Cyclohexanecarbonyl)-2-iodo-1-phenylpyrrolo[1,2-*a*]-quinoline-4-carbaldehyde (8i). The product was obtained as a yellow crystals (88.7 mg, 70% yield): mp 120−122 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.87 (s, 1H), 7.73−7.70 (m, 2H), 7.51−7.49 (m, 3H), 7.34−7.32 (m, 2H), 7.26 (t, J = 7.3 Hz, 1H), 7.16−7.14 (m, 1H), 7.07 (d, J = 8.0 Hz, 1H), 3.03−2.97 (m, 1H), 2.03−2.00 (m, 2H), 1.77−1.76 (m, 2H), 1.55−1.46 (m, 2H), 1.27−1.19 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.6, 188.3, 134.8, 134.7, 132.6, 132.0, 131.2, 130.9, 130.7, 129.5, 129.3, 126.6, 124.9, 123.1, 122.5, 118.0, 52.0, 28.5,

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26.0; HRMS (ESI) calcd for $[C_{26}H_{22}INO_2]$ requires $[M]^+$ 507.0695, found $[M]^+$ 507.0696.

3-(4-Ethylbenzoyl)-2-iodo-7-methoxy-1-phenylpyrrolo[1,2-*a*]quinoline-4-carbaldehyde (8j). The product was obtained as a orange crystals (111.8 mg, 80% yield): mp 140−142 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.79 (s, 1H), 7.87 (d, J = 8.0 Hz, 2H), 7.66 (s, 1H), 7.56−7.54 (m, 3H), 7.43−7.41 (m, 2H), 7.27 (d, J = 8.8 Hz, 2H), 7.17 (d, J = 2.9 Hz, 1H), 7.12 (d, J = 9.5 Hz, 1H), 6.84 (dd, J = 2.9 and 9.5 Hz, 1H), 3.83 (s, 3H), 2.70 (q, J = 7.3 Hz, 2H), 1.25 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.4, 188.0, 156.1, 149.9, 136.2, 134.4, 131.9, 131.3, 131.2, 130.3, 129.4, 129.3, 128.0, 126.5, 125.6, 124.3, 121.0, 119.4, 119.3, 111.6, 55.6, 29.0, 15.0. HRMS (ESI) calcd for $[C_{29}H_{22}INO_3]$ requires $[M]^+$ 559.0644, found 559.0641.

General Procedure for the Synthesis of 1-Benzoyl-2-iodo-3-aryl-indolizine-8-carbaldehyde 9a,b. To a vial 4-alkynl pyranoquinoline **3** (0.25 mmol) and 3.0 equiv of I_2 were added in DCM. The reaction was then stirred at room temperature until TLC revealed complete conversion of the starting material. The solution was washed with saturated solution of $Na_2S_2O_3$ and then extracted with EtOAc. The combined organic layers were dried over Na_2SO_4, concentrated, and purified by column chromatography to afford the corresponding product.

2-Iodo-1-(4-methylbenzoyl)-3-phenylindolizine-8-carbaldehyde (9a). The product was obtained as a yellow solid (81.3 mg, 70% yield): mp 80−82 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.7 (s, 1H), 8.06 (d, J = 8.0 Hz, 1H), 7.76 (d, J = 8.0 Hz, 2H), 7.51−7.47 (m, 2H), 7.45−7.42 (m, 3H), 7.37 (d, J = 6.5 Hz, 1H), 7.20−7.18 (m, 1H), 6.62 (t, J = 6.9 Hz,1H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.0, 188.0, 143.7, 136.2, 131.0, 130.2, 129.9, 129.5, 129.3, 128.7, 128.3, 126.9, 126.5, 118.4, 110.5, 21.8; HRMS (ESI) calcd for $[C_{23}H_{16}INO_2]$ requires $[M]^+$ 465.0226, found $[M]^+$ 465.0227.

2-Iodo-1-(4-methoxybenzoyl)-3-p-tolylindolizine-8-carbaldehyde (9b). The product was obtained as a orange crystals (89.1 mg, 72% yield): mp 102−104 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.81 (s, 1H), 8.09 (dd, J = 1.4 and 5.8 Hz, 1H), 7.88 (dd, J = 2.2 and 6.6 Hz, 2H), 7.41 (dd, J = 1.4 and 6.6 Hz, 1H), 7.36 (s, 4H), 6.91 (dd, J = 2.2 and 6.5 Hz, 2H), 6.65 (t, J = 6.9 Hz, 1H), 3.85 (s, 3H), 2.45 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.3, 188.1, 163.4, 139.6, 132.4, 131.8, 130.9, 130.0, 128.8, 128.3, 126.9, 126.5, 118.2, 113.8, 110.4, 55.4, 21.5; HRMS (ESI) calcd for $[C_{24}H_{18}INO_3]$ requires $[M]^+$ 495.0331, found $[M]^+$ 495.0335.

General Procedure for the Synthesis of Suzuki coupling Product 11. To a vial was added the **8a** (0.20 mmol), 1.2 equiv of (4-methoxyphenyl)boronic acid **10**, 10 mol % $Pd(PPh_3)_2Cl_2$, K_2CO_3 (2.5 equiv) and DMF:H_2O (4:1) (2.0 mL). The reaction vial was then sealed and flushed with nitrogen, and then heated to 80 °C until TLC revealed complete conversion of the starting material. The solution was allowed to cool and diluted with H_2O and then extracted with EtOAc. The combined organic layers were dried over $MgSO_4$, concentrated, and purified by column chromatography to afford the corresponding product.

2-(4-Methoxyphenyl)-3-(4-methylbenzoyl)-1-phenylpyrrolo-[1,2-*a*]quinoline-4-carbaldehyde (11). The product was obtained as a brown solid (74.2 mg, 75% yield): mp 200−201 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.78 (s, 1H), 7.74 (t, J = 7.3 Hz, 3H), 7.68 (s, 1H), 7.32 (t, J = 7.3 Hz, 1H), 7.28−7.21 (m, 5H), 7.16−7.10 (m, 4H), 6.82 (d, J = 8.8 Hz, 2H), 6.47 (d, J = 8.8 Hz, 2H), 3.58 (s, 3H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.4, 188.4, 158.0, 139.4, 138.4, 135.7, 132.3, 131.6, 131.3, 131.1, 130.7, 130.4, 130.3, 129.6, 128.4, 128.0, 127.1, 125.7, 125.1, 124.2, 123.5, 118.2, 117.8, 113.0, 54.9, 21.4; HRMS (ESI) calcd for $[C_{34}H_{25}NO_3]$ requires $[M]^+$ 495.1834, found $[M]^+$ 495.1834.

General Procedure for the Synthesis of Heck coupling Product 13. To a vial was added the **8a** (0.20 mmol), 1.2 equiv of *N*,*N*-dimethylacrylamide (**12**), 10 mol % $Pd(PPh_3)_2Cl_2$, K_3PO_4 (2.5 equiv) and DMF (2.0 mL). The reaction vial was then sealed and flushed with nitrogen, and then heated to 80 °C until TLC revealed complete conversion of the starting material. The solution was allowed to cool and diluted with H_2O and then extracted with EtOAc. The combined organic layers were dried over $MgSO_4$, concentrated, and purified by column chromatography to afford the corresponding product.

(*E*)-3-(4-Formyl-3-(4-methylbenzoyl)-1-phenylpyrrolo[1,2-*a*]quinolin-2-yl)-*N*,*N*-dimethylacrylamide (13). The product was obtained as a brown solid (68.0 mg, 70% yield): mp 160−162 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.70 (s, 1H), 7.93 (d, J = 8.0 Hz, 2H), 7.70 (d, J = 8.0 Hz, 1H), 7.64 (s, 1H), 7.49−7.45 (m, 1H), 7.39−7.35 (m, 2H), 7.27−7.24 (m, 5H), 7.22−7.19 (m, 3H), 6.21 (d, J = 16.1 Hz, 1H), 2.76 (s, 3H), 2.53 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 194.9, 188.2, 166.8, 139.6, 139.1, 135.6, 133.9, 133.3, 133.0, 132.5, 131.0, 130.8, 130.2, 129.5, 129.3, 128.7, 126.8, 126.8, 124.7, 124.6, 122.4, 123.3, 119.4, 118.2, 116.0, 29.7, 29.6, 20.7; HRMS (ESI) calcd for $[C_{32}H_{26}N_2O_3]$ requires $[M + H]^+$ 487.2023, found $[M + H]^+$ 487.2021.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Experimental procedures and copies of HRMS, ^{1}H and ^{13}C NMR spectra for all new compounds. CIF for compounds **6a** and **9b**. 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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