Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Construction of Benzo-fused Indolizines, Pyrrolo[1,2-*a*]quinolines, via Alkyne-Carbonyl Metathesis

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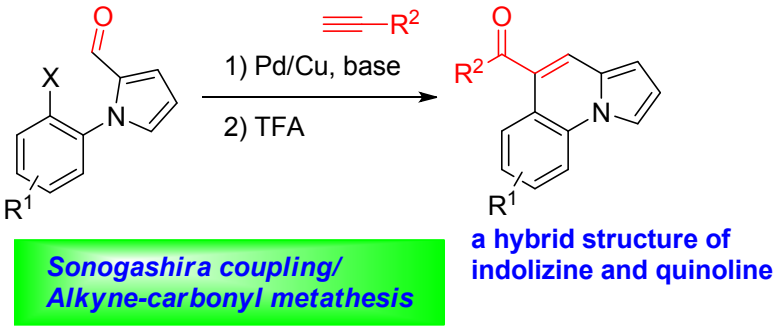


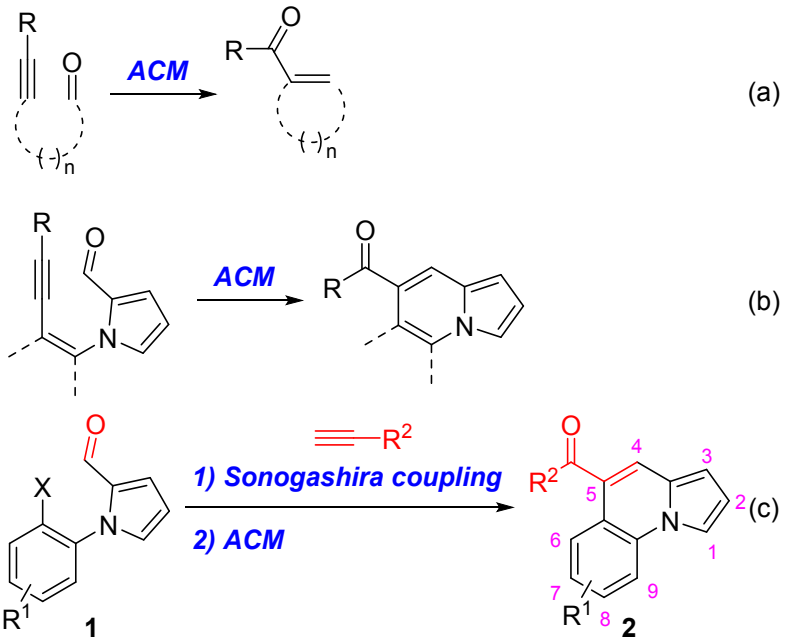
Abstract: Strategic use of a sequential Sonogashira coupling/intramolecular alkyne-carbonyl metathesis process for the synthesis of pyridine ring from 1-(2-haloaryl)-1*H*-pyrrole-2-carbaldehydes allowed ready access to a diverse novel benzo-fused indolizines, pyrrolo[1,2-*a*]quinolines, in good to excellent yields. As a hybrid structure of indolizine and quinoline, the resulting scaffold has an acyl substituent at C5 position, which is difficult to make by any other known approaches.

Keywords: Hybrid Structure; Pyrrolo[1,2-*a*]quinoline; Indolizine; Quinoline; Sonogashira coupling; Alkyne-carbonyl metathesis; Diversity-oriented synthesis.

Introduction

Alkyne-carbonyl metathesis (ACM) is a synthetic transformation that α,β–unsaturated carbonyl compounds arise from alkyne and carbonyl functional groups through a [2+2] cycloaddition and cycloreversion process.[1] As the resulting α,β–unsaturated carbonyl group is a highly versatile functionality, this reaction often provides an opportunity for domino processes by its being coupled with other subsequent reactions such as Nazarov cyclization and intramolecular aza-Michael addition.[2] Another interesting feature of ACM is that it allows facile access to a number of carbo- and heterocycles when these two functional groups are appropriately linked (Scheme 1(a)). Indeed, construction of several ring systems such as cycloalkenone and chromenone was realized by this concept.[3]

Scheme 1. Synthetic Approach to Indolizine via ACM



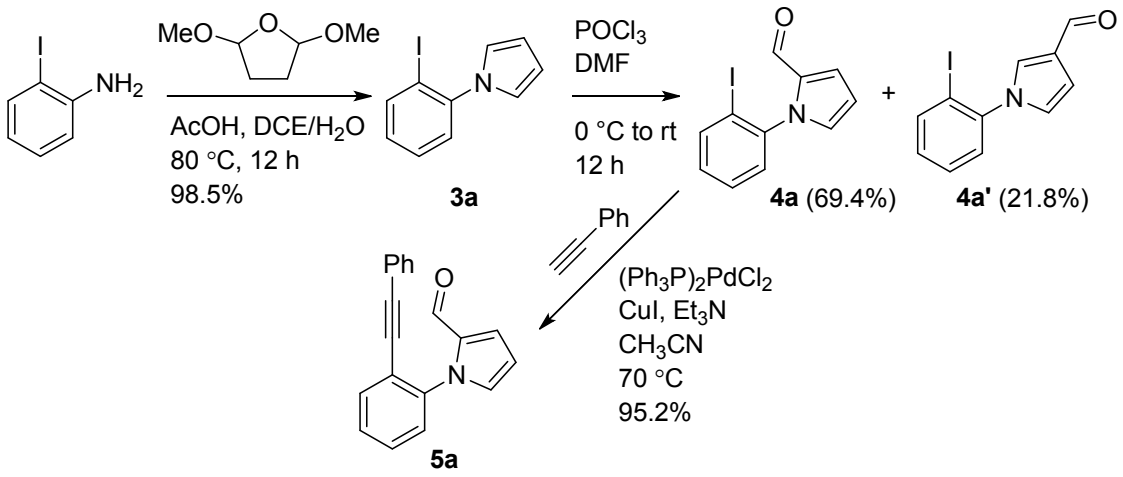
In connection with our research interest on design and synthesis of novel indolizines with distinctive substitution pattern,[4] we wish to employ intramolecular ACM reaction to gain access to a pyridine moiety of indolizine from pyrrole-2-carboxaldehydes possessing a suitably situated triple bond (Scheme 1(b)). For this purpose, we envisioned that 1-(2-iodoaryl)-1*H*-pyrrole-2-carbaldehydes would be converted to benzo-fused indolizines, pyrrolo[1,2-*a*]quinolines, through a sequential Sonogashira coupling/intramolecular ACM process (Scheme 1(c)). The resulting product **2** can be viewed as a hybrid structure[5] of 7-acylindolizine[6] and 4-acylquinoline,[7] two important pharmacophores, which would be useful for biological screening.[8] Previous syntheses of this skeleton have been disclosed in the literature.[9] For example, Fürstner developed hydroarylation of alkyne-containing biaryl derivatives and Lautens applied palladium-catalyzed annulation of aryl heterocycles with strained alkenes to get access to this backbone, respectively. More recently, Wang reported the synthesis of pyrrolo[1,2-*a*]quinolines via Ce(III)-catalyzed [3+2] annulation of 2-alkylazaarenes with nitroolefins. Notably, while there are several methods which enable installation of aryl, alkyl, or acyl group at C4 site of this nucleus, construction of pyrrolo[1,2-*a*]quinolines bearing an acyl group at C5 position has been very rare.[10]

Results and discussion

The required 1-(2-iodoaryl)-1*H*-pyrrole-2-carbaldehydes **1** for this study were prepared by adopting a procedure consisting of Paal-Knorr pyrrole synthesis and Vilsmeier Haack formylation (Scheme 2).[11] Thus, acid-catalyzed reaction of 2-iodoaniline and 2,5-dimethoxytetrahydrofuran cleanly afforded the desired pyrrole **3a**, which was converted to **4a** along with **4a'** upon subsequent formylation. Sonogashira coupling reaction of **4a** with

phenylacetylene occurred in acetonitrile as solvent at 70 °C, furnishing the coupled product **5a** in 95.2% yield.

Scheme 2. Synthesis of 5[a]

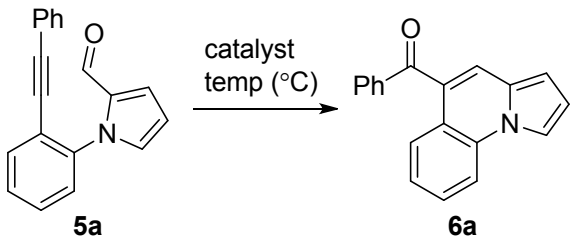


[a] A mixture of 2-iodoaniline (4.57 mmol), 2,5-dimethoxytetrahydrofuran (0.62 mL, 1.05 equiv), and AcOH (0.32 mL, 1.22 equiv) in DCE (8.5 mL) and H_2O (5.0 mL) was heated at 80 °C. A mixture of **3a** (3.72 mmol) and $POCl_3$ (0.69 mL, 2.0 equiv) in DMF (4 mL) was stirred at rt. A mixture of **4a** (0.4 mmol), phenylacetylene (0.049 mL, 1.1 equiv), $(Ph_3P)_2PdCl_2$ (14 mg, 0.05 equiv), CuI (3.9 mg, 0.05 equiv), and Et_3N (0.113 mL, 2.0 equiv) in CH_3CN (1.5 mL) was heated at 70 °C.

Optimal conditions for ACM via exposure of **5a** to several acidic media were then examined and the results are summarized in Table 1. When **5a** was treated with either catalytic or stoichiometric amount of BF_3-Et_2O at rt, no reaction occurred (entries 1 and 2). Elevating the reaction temperature to 80 °C gave the desired product **6a** in 30% yield while increasing the amount of BF_3-Et_2O to 1.5 equiv did not result in better chemical yield (entries 3 and 4). Use of other Lewis acids such as $In(OTf)_3$, $InCl_3$, or AgOTf provided the similar results (entries 5-7). To our delight, reaction of **5a** in formic acid at 100 °C furnished **6a** in 62% yield (entry

8). Finally, we were pleased to find that the desired product was cleanly obtained under TFA at 90 °C (entry 9).

Table 1. Reaction Optimization for Alkyne-Aldehyde Metathesis[a]



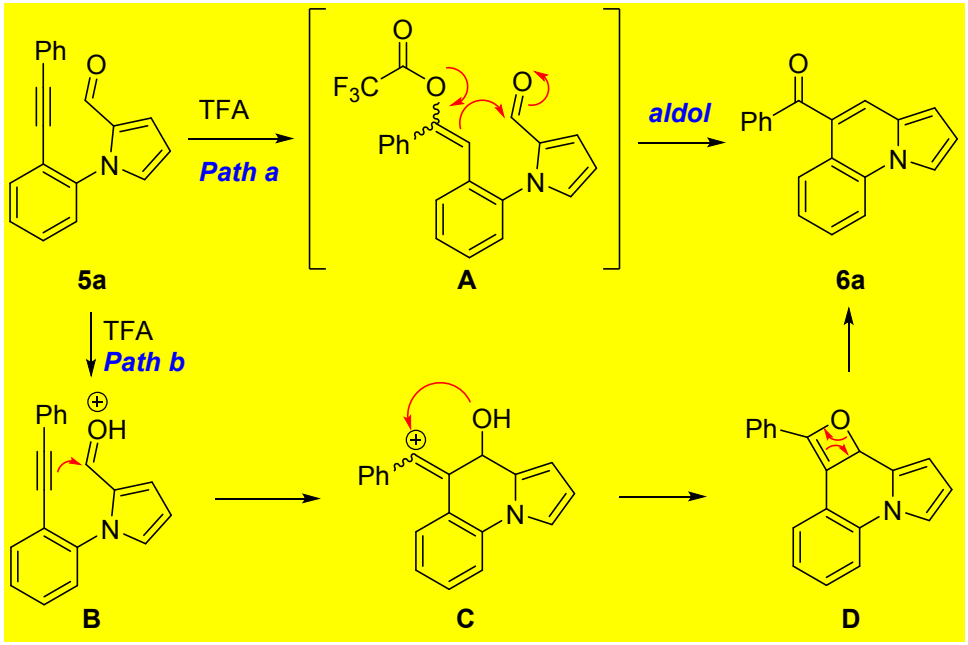
5a **6a**

entry	catalyst (equiv)	temperature	time (hr)	solvent	yield (%)[b]
1	BF_3-Et_2O (0.5)	rt	12	DCE	n.r.
2	BF_3-Et_2O (1.2)	rt	12	DCE	n.r.
3	BF_3-Et_2O (1.2)	80	16	DCE	30
4	BF_3-Et_2O (1.5)	70	16	DCE	28
5	$In(OTf)_3$ (0.2)	80	16	DCE	23
6	$InCl_3$ (1.5)	80	12	DCE	22
7	AgOTf (1.5)	80	12	DCE	15
8	HCO_2H	100	0.5	-[c]	62
9	TFA	90	1	-[c]	99

[a] A mixture of **5a** (0.1 mmol) and catalyst in solvent (0.5 mL) was stirred at the indicated temperature and time unless otherwise noted. [b] Isolated yield (%) [c] Formic acid or TFA was used as solvent.

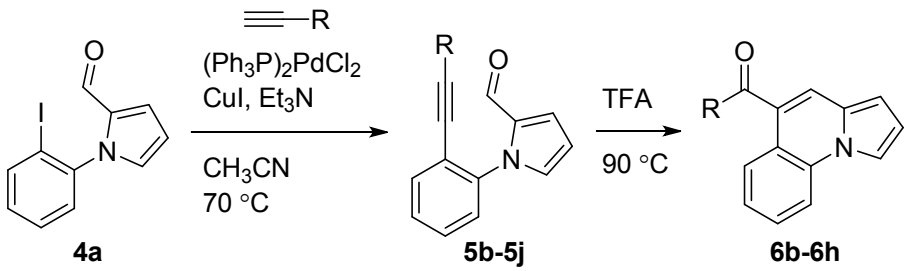
Formation of **6a** from **5a** can be rationalized based on the mechanism previously proposed (Scheme 3). Addition of TFA to the alkyne unit in **5a** would generate **A**, which then undergoes intramolecular aldol/dehydration to give rise to **6a**. Alternatively, it can be understood via alkyne addition to aldehyde promoted by initial protonation (**B**). Attack of the resulting carbocation by the neighboring hydroxyl group (**C**) followed by [2+2] cycloreversion (**D**) would lead to **6a**.

Scheme 3. Proposed ACM Mechanism



Having established a new and efficient synthetic route to pyrrolo[1,2-*a*]quinoline skeleton by way of a sequential Sonogashira coupling/ACM procedure, we first examined the reaction scope by reacting **4a** with several other alkynes (Scheme 4). Under optimized conditions, several alkynes were installed to afford the corresponding **5b-5j** in good yields. Submission of the resulting coupled products **5b-5g** to TFA led to the desired cyclized compounds **6b-6g** in excellent yields (entries 1-6). Electron density of the aryl moiety in **5** did not seem to affect the reaction efficiency. ACM of substrate having a heteroaryl group such as thiophene proceeded well to give the corresponding product (entry 5). Using a mixture of TFA/DCE (1:1) provided better isolated yields in cases of **5d-5g** than using neat TFA. However, exposure of cyclohexene-containing substrate **5h** to these conditions provided **6h** in low yield presumably due to decomposition of the product (entry 7). Unfortunately, little or no conversion was observed with compounds possessing a cyclopentyl or n-butyl group (entries 8 and 9).

Scheme 4. Synthesis of Diverse Pyrrolo[1,2-*a*]quinolines via Reactions of 4a with Several Alkynes[a]

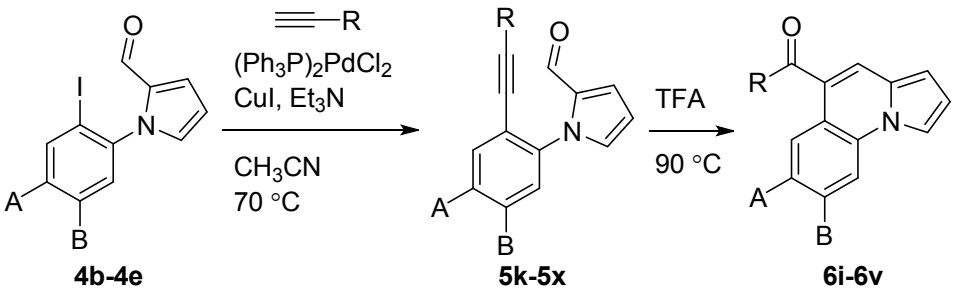


entry	alkyne (R)	**5** (%)[b]	**6** (%)[b]
1	4-FC_6H_4	**5b** (90.8)	**6b** (92.7)
2	3-FC_6H_4	**5c** (91.3)	**6c** (82.8)
3	3-MeC_6H_4	**5d** (75.8)	**6d** (82)[c]
4	4-$MeOC_6H_4$	**5e** (71.7)	**6e** (84)[c]
5	3-thiophene	**5f** (74.3)	**6f** (81)[c]
6	6-MeO-2-naphthalene	**5g** (63.6)	**6g** (87)[c]
7	1-cyclohexene	**5h** (95)	**6h** (32.6)
8	cyclopentyl	**5i** (77.4)	trace
9	n-Bu	**5j** (77.3)	n.r.

[a] A mixture of **4a** (0.4 mmol), alkyne (1.1 equiv), $(Ph_3P)_2PdCl_2$ (14 mg, 0.05 equiv), CuI (3.9 mg, 0.05 equiv), and Et_3N (0.11 mL, 2.0 equiv) in CH_3CN (1.5 mL) was heated at 70 °C. A mixture of **5** (0.1 mmol) in TFA (0.5 mL) was stirred at 90 °C unless otherwise stated. [b] Isolated yield (%) [c] A mixture of **5** (0.1 mmol) in TFA/DCE (1:1, 1 mL) was stirred at 90 °C.

Generality of this reaction was further investigated by exposing several other **4b-4e**[12] to these conditions (Scheme 5). Irrespective of the electronic properties of iodoaryl rings, the whole sequence proceeded smoothly to give the products in good yields except for the cases of ACM reactions of substrates bearing a cyclohexene unit, **5o** and **5t**.

Scheme 5. Synthesis of Diverse Pyrrolo[1,2-*a*]quinolines via Reactions of 4b-4e with Several Alkynes[a]



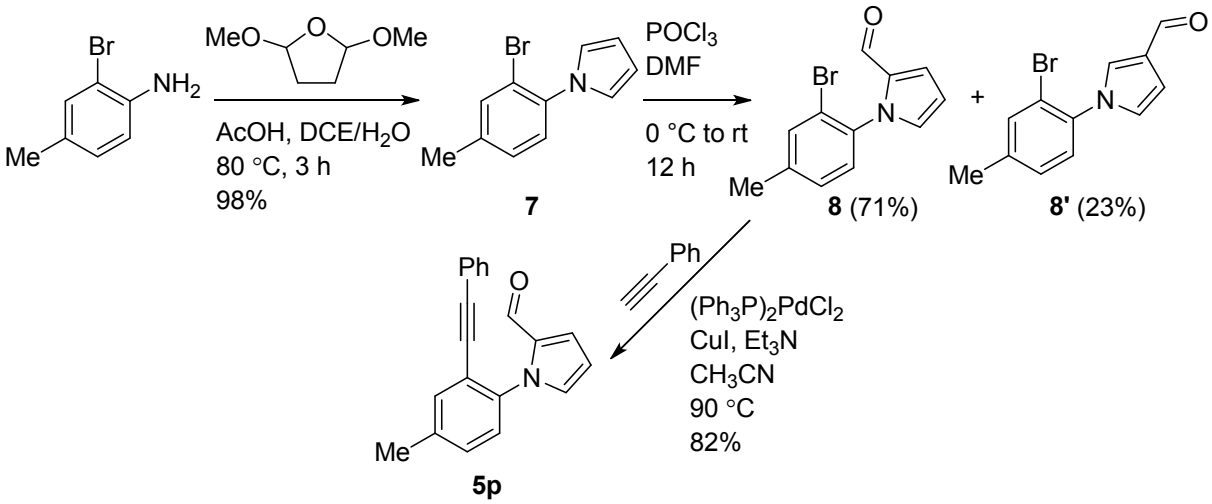
4b-4e **5k-5x** **6i-6v**

entry	**4**	alkyne (R)	**5** (%)[b]	**6** (%)[b]
1	**4b** (A = H, B = Cl)	Ph	**5k** (90.3)	**6i** (83.5)
2	**4b**	4-FC_6H_4	**5l** (86.2)	**6j** (77)
3	**4b**	4-$MeOC_6H_4$	**5m** (83.2)	**6k** (86)
4	**4b**	3-thiophene	**5n** (69.4)	**6l** (84)
5	**4b**	1-cyclohexene	**5o** (72)	**6m** (34.6)[c]
6	**4c** (A = Me, B = H)	Ph	**5p** (92.2)	**6n** (86.2)
7	**4c**	4-FC_6H_4	**5q** (82)	**6o** (89.5)
8	**4c**	4-$MeOC_6H_4$	**5r** (83.6)	**6p** (82.7)
9	**4c**	3-thiophene	**5s** (89.5)	**6q** (83.6)
10	**4c**	1-cyclohexene	**5t** (85.2)	**6r** (34)[c]
11	**4d** (A = CO_2Me, B = H)	Ph	**5u** (83.3)	**6s** (88)
12	**4d**	4-$MeOC_6H_4$	**5v** (85.7)	**6t** (82)
13	**4e** (A = NO_2, B = H)	Ph	**5w** (82.2)	**6u** (86)
14	**4e**	3-MeC_6H_4	**5x** (80)	**6v** (88.2)

[a] A mixture of **4b-4e** (0.36 mmol), alkyne (1.1 equiv), $(Ph_3P)_2PdCl_2$ (0.05 equiv), CuI (0.05 equiv), and Et_3N (2.0 equiv) in CH_3CN (1.5 mL) was heated at 70-80 °C. A mixture of **5** (0.1 mmol) in TFA (0.5 mL) was stirred at 90 °C unless otherwise stated. [b] Isolated yield (%) [c] A mixture of **5** (0.1 mmol) in TFA/DCE (1:1, 1 mL) was stirred at 90 °C.

In addition, the chemistry described above was applied to 2-bromo-4-methylaniline to expand the substrate scope (Scheme 6). Thus, 1-(2-bromo-4-methylphenyl)-1*H*-pyrrole-2-carbaldehyde **8** was prepared by following the similar procedure for **4a**. Again, **8** underwent Sonogashira cross-coupling with phenylacetylene to furnish **5p** in 82% yield.

Scheme 6. Use of 2-Bromoaniline for the Synthesis of 5p[a]



[a] A mixture of 2-bromo-4-methylaniline (2.69 mmol), 2,5-dimethoxytetrahydrofuran (0.37 mL, 1.05 equiv), and AcOH (0.15 mL, 1.22 equiv) in DCE (4 mL) and H_2O (2.5 mL) was heated at 80 °C. A mixture of **7** (1.06 mmol) and $POCl_3$ (0.2 mL, 2.0 equiv) in DMF (2 mL) was stirred at rt. A mixture of **8** (0.19 mmol), phenylacetylene (0.02 mL, 1.1 equiv), $(Ph_3P)_2PdCl_2$ (13 mg, 0.1 equiv), CuI (3.6 mg, 0.1 equiv), and Et_3N (0.053 mL, 2.0 equiv) in CH_3CN (1 mL) was heated at 90 °C.

In summary, we have accomplished a highly efficient synthesis of a novel benzo-fused indolizines, pyrrolo[1,2-*a*]quinolines, by way of a sequential Sonogashira cross-coupling/intramolecular alkyne-carbonyl metathesis process to construct the central pyridine ring. Several 1-(2-haloaryl)-1*H*-pyrrole-2-carbaldehydes readily prepared by way of Paal-Knorr pyrrole ring synthesis and subsequent Vilsmeier Haack formylation of commercially available 2-haloanilines were successfully converted to various pyrrolo[1,2-*a*]quinolines with an acyl substituent at C5 site, which cannot be accessed by any other synthetic methods. Unprecedented substitution pattern of this nucleus should be useful to explore its various biological functions. Application of this protocol for the synthesis of other heterocycles as well as investigation on utility of these compounds are currently in progress.

Experimental Section

General Methods

Unless specified, all reagents and starting materials were purchased from commercial sources and used as received without purification. "Concentrated" refers to the removal of volatile solvents via distillation using a rotary evaporator. "Dried" refers to pouring onto, or passing through, anhydrous magnesium sulfate followed by filtration. Flash chromatography was performed using silica gel (230−400 mesh) with hexanes, ethyl acetate, and dichloromethane as eluent. All reactions were monitored by thin-layer chromatography on 0.25 mm silica plates (F-254) visualizing with UV light. ^{1}H and ^{13}C NMR spectra were recorded on 400 MHz NMR spectrometer and were described as chemical shifts, multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet), coupling constant in hertz (Hz), and number of protons. IR spectra were recorded on FT-IR using diamond ATR technique and were described as wavenumbers (cm^{-1}). HRMS were measured with electrospray ionization (ESI) and Q-TOF mass analyzer.

Representative Procedure for the Synthesis of 3a

To a stirred solution of 2-iodoaniline (1 g, 4.57 mmol), AcOH (0.32 mL, 1.22 equiv) and H_2O (5.0 mL) in DCE (8.5 mL) at 80 °C was added 2,5-dimethoxytetrahydrofuran (0.62 mL, 1.05 equiv) in one portion and heating was continued at 80 °C for 12 h. After cooling, layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2 x 30 mL). The combined organic layer was dried over anhydrous $MgSO_4$ and concentrated under reduced pressure to afford the crude product which was purified by flash chromatography on silica gel (hexanes: EtOAc, 95:5) to furnish **3a** as colorless oil (1.21 g, 98.5%).

1-(2-Iodophenyl)-1*H*-pyrrole (3a). Brown oil (1.21 g, 98.5%), **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.94 (dd, *J* = 1.1, 8.1 Hz, 1H), 7.39-7.43 (m, 1H), 7.31 (dd, *J* = 1.4, 7.8 Hz, 1H), 7.10 (dt, *J*

= 1.6, 7.9 Hz, 1H), 6.82 (t, *J* = 2.1 Hz, 2H), 6.34 (t, *J* = 2.1 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 144.1, 140.0, 129.5, 129.0, 128.1, 122.2, 109.2, 95.9; **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{10}H_9IN$ 269.9774, found 269.9785.

3b-3d were prepared by following the similar procedure for **3a**.

1-(5-Chloro-2-iodophenyl)-1*H*-pyrrole (3b). Brown oil (1.14 g, 95%), **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.5 Hz, 1H), 7.31 (d, *J* = 2.4 Hz, 1H), 7.11 (dd, *J* = 2.4, 8.4 Hz, 1H), 6.81 (t, *J* = 2.0 Hz, 2H), 6.35 (t, *J* = 2.0 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 145.1, 140.8, 135.0, 129.6, 128.4, 122.1, 109.8, 92.9; **HRMS** (ESI-QTOF) *m/z* $[M+Na]^+$ calcd for $C_{10}H_7ClINNa$ 325.9204, found 325.9215.

1-(2-Iodo-4-methylphenyl)-1*H*-pyrrole (3c). Brown oil (2.41 g, 99.2%), **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.77 (s, 1H), 7.18-7.22 (m, 2H), 6.79 (t, *J* = 1.9 Hz, 2H), 6.33 (t, *J* = 2.0 Hz, 2H), 2.38 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 141.6, 140.3, 139.7, 129.7, 127.6, 122.3, 109.0, 95.9, 20.6; **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{11}H_{11}IN$ 283.9931, found 283.9924.

Methyl 3-iodo-4-(1*H*-pyrrol-1-yl)benzoate (3d). White solid, mp: 110.3-111.8 °C (412 mg, 97%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.61 (d, *J* = 1.6 Hz, 1H), 8.06 (dd, *J* = 1.6, 8.2 Hz, 1H), 7.33 (d, *J* = 8.2 Hz, 1H), 6.86 (t, *J* = 1.8 Hz, 2H), 6.36 (t, *J* = 1.9 Hz, 2H), 3.95 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 165.0, 147.6, 141.6, 130.7, 130.3, 127.6, 122.0, 110.0, 94.4, 52.7; **IR** (ATR) ν = 3127, 2949, 1714, 1499, 1288, 1112 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{12}H_{11}INO_2$ 327.9829, found 327.9844.

Procedure for the Synthesis of 3e

To a gently refluxing mixture of 4-nitroaniline (0.25 g, 0.95 mmol), and sodium acetate (0.435 mg, 5.3 mmol) in acetic acid (2 ml) was added 2,5-dimethoxytetrahydrofuran (0.13 mL, 1.04 mmol) and the reaction was continued for 3 h. Then crushed ice was added to the reaction mixture, basified with 1 N sodium hydroxide solution, and extracted with CH_2Cl_2 (3 x 10 mL). The combined organic layer was dried over anhydrous $MgSO_4$ and concentrated under reduced pressure to afford the crude product which was purified by flash chromatography on silica gel (hexanes: EtOAc, 95:5) to furnish **3e** as a yellow solid (0.291 mg, 98.0%).

1-(2-Iodo-4-nitrophenyl)-1*H*-pyrrole (3e). Yellow solid, mp: 102.7-103.8 °C (291.4 mg, 98%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.81 (d, J = 2.1 Hz, 1H), 8.28 (dd, J = 2.0, 8.6 Hz, 1H), 7.40 (d, J = 8.6 Hz, 1H), 6.90 (s, 2H), 6.40 (s, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 149.2, 146.7, 135.7, 127.8, 124.2, 121.9, 110.7, 93.9; **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{10}H_8IN_2O_2$ 314.9625, found 314.9618.

Representative Procedure for the Synthesis of 4a

To a stirred solution of **3a** (1 g, 3.72 mmol) in DMF (4 mL) at 0 °C was dropwise added $POCl_3$ (0.69 mL, 7.43 mmol). After being stirred at rt for 12 h the reaction mixture was neutralized with aq. Na_2CO_3 solution at 0 °C. The aqueous layer was extracted with EtOAc (3 x 50 mL). The combined organic layer was washed with water (2 x 20 mL) and brine (20 mL), dried over anhydrous $MgSO_4$, and concentrated under reduced pressure to afford the crude product, which was purified by flash chromatography on silica gel (hexanes: EtOAc, 9:1) to furnish **4a** as a white solid (0.766 g, 69.4%).

1-(2-Iodophenyl)-1*H*-pyrrole-2-carbaldehyde (4a). White solid, mp: 115.3-115.9 °C (766

mg, 69.4%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.48 (s, 1H), 7.93 (d, *J* = 7.9 Hz, 1H), 7.45 (t, *J* = 7.6 Hz, 1H), 7.34 (d, *J* = 7.8 Hz, 1H), 7.18 (t, *J* = 7.7 Hz, 1H), 7.13 (d, *J* = 1.6 Hz, 1H), 6.93 (s, 1H), 6.45 (s, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 178.7, 142.3, 139.6, 132.7, 130.8, 130.5, 129.1, 128.5, 122.0, 111.1, 97.7; **IR** (ATR) ν = 3101, 2879, 1651, 1479, 1384, 1095 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{11}H_9INO$ 297.9723, found 297.9725.

1-(5-Chloro-2-iodophenyl)-1*H*-pyrrole-2-carbaldehyde (4b). White solid, mp: 141.9-142.6 °C (792 mg, 72.5%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.51 (s, 1H), 7.83 (d, *J* = 8.4 Hz, 1H), 7.33 (d, *J* = 2.3 Hz, 1H), 7.18 (dd, *J* = 2.3, 8.5 Hz, 1H), 7.11 (dd, *J* = 1.4, 4.0 Hz, 1H), 6.91 (s, 1H), 6.46 (dd, *J* = 2.8, 3.8 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 178.5, 143.6, 140.2, 134.9, 132.6, 130.71, 130.68, 128.7, 122.9, 111.4, 95.1; **IR** (ATR) ν = 3074, 2804, 1656, 1476, 1355, 1091 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{11}H_8ClINO$ 331.9334, found 331.9340.

1-(2-Iodo-4-methylphenyl)-1*H*-pyrrole-2-carbaldehyde (4c). White solid, mp: 73.7-74.2 °C (1.56 g, 71.2%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.46 (s, 1H), 7.75 (s, 1H), 7.19-7.25 (m, 2H), 7.11 (dd, *J* = 1.2, 3.8 Hz, 1H), 6.90 (s, 1H), 6.43 (t, *J* = 3.2 Hz, 1H), 2.39 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 178.8, 140.9, 140.0, 139.7, 132.7, 130.98, 129.8, 127.98, 110.9, 97.4, 20.8; **IR** (ATR) ν = 3102, 2794, 1657, 1493, 1356, 1099 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$calcd for $C_{12}H_{11}INO$ 311.9880, found 311.9882.

Methyl 4-(2-formyl-1*H*-pyrrol-1-yl)-3-iodobenzoate (4d). White solid, mp: 148.1-148.9 °C (185 mg, 74.1%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.51 (s, 1H), 8.58 (d, *J* = 1.3 Hz, 1H), 8.10

(dd, J = 1.4, 8.1 Hz, 1H), 7.37 (d, J = 8.2 Hz, 1H), 7.13 (d, J = 2.6 Hz, 1H), 6.93 (s, 1H), 6.48 (t, J = 3.2 Hz, 1H), 3.96 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 178.5, 164.9, 146.5, 140.8, 132.6, 131.9, 130.6, 130.3, 128.3, 123.2, 111.5, 97.3, 52.8; **IR** (ATR) ν = 3133, 2834, 1708, 1656, 1282, 1118 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{13}H_{11}INO_3$ 355.9778, found 355.9780.

1-(2-Iodo-4-nitrophenyl)-1*H*-pyrrole-2-carbaldehyde (4e). White solid, mp: 120.5-121.8 °C (250 mg, 85.7%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.56 (s, 1H), 8.76 (d, J = 2.2 Hz, 1H), 8.30 (dd, J = 2.3, 8.6 Hz, 1H), 7.46 (d, J = 8.6 Hz, 1H), 7.16 (d, J = 3.8 Hz, 1H), 6.94 (s, 1H), 6.52 (t, J = 3.2 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 178.5, 148.5, 147.6, 134.6, 132.5, 130.5, 128.7, 124.2, 124.1, 111.98, 97.5; **IR** (ATR) ν = 3111, 2841, 1663, 1517, 1340, 1097 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{11}H_8IN_2O_3$ 342.9574, found 342.9567.

Representative Procedure for the Synthesis of 5a

To a flask charged with **4a** (0.12 g, 0.4 mmol), $(PPh_3)_2PdCl_2$ (0.014 g, 0.02 mmol), CuI (0.0039 g, 0.02 mmol) and phenyl acetylene (0.049 mL, 0.44 mmol) in acetonitrile (1.5 mL) was added Et_3N (0.113 mL, 0.8 mmol) at rt. After being stirred at 70 °C under nitrogen atmosphere for 12 h, the reaction mixture was concentrated *in vacuo* to yield the crude product, which was purified by flash chromatography on silica gel (hexanes: EtOAc, 9:1) to give **5a** as an off white solid (0.104 g, 95.2%).

1-(2-(Phenylethynyl)phenyl)-1*H*-pyrrole-2-carbaldehyde (5a). Off white solid, mp: 55.3-57.2 °C (104.5 mg, 95.2%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.54 (s, 1H), 7.63-7.66 (m, 1H), 7.43-7.47 (m, 2H), 7.37-7.41 (m, 1H), 7.28-7.29 (m, 5H), 7.20 (dd, J = 1.5, 3.9 Hz, 1H), 7.12 (d, J = 1.9 Hz, 1H), 6.47 (dd, J = 2.7, 3.8 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 179.0,

140.4, 133.4, 132.6, 131.6, 131.2, 128.97, 128.74, 128.67, 128.4, 127.5, 126.2, 122.6, 122.1, 110.7, 94.2, 85.0; **IR** (ATR) ν = 3060, 2793, 1665, 1498, 1412, 1083 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{19}H_{14}NO$ 272.1070, found 272.1059.

1-(2-((4-Fluorophenyl)ethynyl)phenyl)-1*H*-pyrrole-2-carbaldehyde (5b). Colorless gum (150.3 mg, 90.8%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.53 (s, 1H), 7.60-7.64 (m, 1H), 7.42-7.47 (m, 2H), 7.38-7.41 (m, 1H), 7.21-7.27 (m, 2H), 7.18 (dd, *J* = 1.6, 4.0 Hz, 1H), 7.09 (t, *J* = 1.9 Hz, 1H), 6.97 (t, *J* = 8.7 Hz, 2H), 6.46 (dd, *J* = 2.7, 3.8 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 179.1, 162.8 (d, *J* = 248.9 Hz), 140.4, 133.5 (d, *J* = 8.4 Hz), 133.4, 132.5, 131.2, 129.1, 128.7, 127.6, 121.9, 118.71, 118.68, 115.8 (d, *J* = 22.0 Hz), 110.7, 93.1, 84.7; **IR** (ATR) ν = 3068, 2794, 1666, 1508, 1222, 1084 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{19}H_{13}FNO$ 290.0976, found 290.0976.

1-(2-((3-Fluorophenyl)ethynyl)phenyl)-1*H*-pyrrole-2-carbaldehyde (5c). Colorless gum (133.4 mg, 91.3%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.54 (s, 1H), 7.63-7.66 (m, 1H), 7.44-7.49 (m, 2H), 7.39-7.42 (m, 1H), 7.19-7.25 (m, 2H), 7.10 (s, 1H), 6.93-7.05 (m, 3H), 6.48 (t, *J* = 3.2 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 178.97, 162.4 (d, *J* = 245.1 Hz), 140.7, 133.4, 132.7, 131.3, 130.0 (d, *J* = 8.7 Hz), 129.4, 128.7, 127.6, 127.5 (d, *J* = 3.0 Hz), 124.4 (d, *J* = 9.3 Hz), 121.6, 121.3, 118.3 (d, *J* = 22.7 Hz), 116.1 (d, *J* = 21.2 Hz), 110.8, 92.7, 85.9; **IR** (ATR) ν = 3065, 2793, 1666, 1498, 1204, 1084 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{19}H_{13}FNO$ 290.0976, found 290.0969.

1-(2-(m-Tolylethynyl)phenyl)-1*H*-pyrrole-2-carbaldehyde (5d). Colorless gum (87.3 mg,

75.8%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.53 (s, 1H), 7.64 (t, *J* = 4.5 Hz, 1H), 7.43-7.45 (m, 2H), 7.37-7.39 (m, 1H), 7.19 (d, *J* = 3.0 Hz, 1H), 7.15 (d, *J* = 7.5 Hz, 1H), 7.06-7.11 (m, 4H), 6.46 (s, 1H), 2.30 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 178.9, 140.3, 137.98, 133.3, 132.5, 132.0, 131.2, 129.6, 128.8, 128.7, 128.6, 128.2, 127.5, 122.3, 122.0, 120.8, 110.6, 94.4, 84.6, 21.3; **IR** (ATR) ν = 3059, 2792, 1665, 1496, 1314, 1083 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+Na]^+$ calcd for $C_{20}H_{15}NNaO$ 308.1046, found 308.1051.

1-(2-((4-Methoxyphenyl)ethynyl)phenyl)-1*H*-pyrrole-2-carbaldehyde (5e). Colorless gum (80 mg, 71.7%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.52 (s, 1H), 7.62 (s, 1H), 7.39-7.42 (m, 3H), 7.19-7.21 (m, 3H), 7.10 (s, 1H), 6.80 (d, *J* = 8.0 Hz, 2H), 6.46 (s, 1H), 3.79 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 179.1, 160.0, 140.1, 133.4, 133.1, 132.4, 131.2, 128.65, 128.58, 127.5, 122.4, 120.6, 114.7, 114.1, 110.7, 94.4, 83.8, 55.4; **IR** (ATR) ν = 3109, 2837, 1664, 1509, 1245, 1083 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+Na]^+$ calcd for $C_{20}H_{15}NNaO_2$ 324.0995, found 324.1005.

1-(2-(Thiophen-3-ylethynyl)phenyl)-1*H*-pyrrole-2-carbaldehyde (5f). Off white solid; mp: 95.0-95.8 °C (83.2 mg, 74.3%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.53 (s, 1H), 7.62 (s, 1H), 7.39-7.44 (m, 3H), 7.32 (s, 1H), 7.18-7.22 (m, 2H), 7.10 (s, 1H), 6.96 (s, 1H), 6.45 (s, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 179.1, 140.4, 133.4, 132.4, 131.2, 129.7, 129.4, 128.9, 128.7, 127.6, 125.5, 122.0, 121.7, 120.8, 110.7, 89.5, 84.6; **IR** (ATR) ν = 3149, 2925, 1641, 1511, 1262, 1091 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{17}H_{12}NOS$ 278.0634, found 278.0634.

1-(2-((6-Methoxynaphthalen-2-yl)ethynyl)phenyl)-1*H*-pyrrole-2-carbaldehyde (5g). Off white solid; mp: 98.1-98.8 °C (90.3 mg, 63.6%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.56 (s, 1H), 7.61-7.72 (m, 4H), 7.40-7.47 (m, 3H), 7.22-7.24 (m, 2H), 7.13-7.15 (m, 2H), 7.08 (s, 1H), 6.50 (s, 1H), 3.92 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 179.1, 158.5, 140.3, 134.4, 133.4, 132.5, 131.5, 131.3, 129.5, 128.8, 128.7, 128.6, 128.4, 127.5, 126.9, 122.2, 120.8, 119.5, 117.4, 110.7, 105.9, 94.9, 84.7, 55.4; **IR** (ATR) ν = 3148, 2919, 1643, 1429, 1262, 1113 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{24}H_{18}NO_2$ 352.1332, found 352.1336.

1-(2-(Cyclohexenylethynyl)phenyl)-1*H*-pyrrole-2-carbaldehyde(5h). Colorless oil (132 mg, 95%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.47 (s, 1H), 7.51-7.54 (m, 1H), 7.37-7.40 (m, 2H), 7.32-7.34 (m, 1H), 7.14-7.15 (m, 1H), 7.04 (s, 1H), 6.41 (t, *J* = 3.1 Hz, 1H), 5.99 (s, 1H), 2.05-2.06 (m, 2H), 1.97 (br s, 2H), 1.54 (br s, 2H), 1.59 (br s, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 179.1, 140.0, 136.3, 133.2, 132.4, 130.96, 128.5, 128.4, 127.4, 122.5, 120.4, 110.6, 96.3, 82.4, 28.6, 25.8, 22.2, 21.4; **IR** (ATR) ν = 3112, 2927, 1665, 1494, 1333, 1082 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{19}H_{18}NO$ 276.1383, found 276.1383.

1-(2-(Cyclopentylethynyl)phenyl)-1*H*-pyrrole-2-carbaldehyde (5i). Colorless oil (82.3 mg, 77.4%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.45 (s, 1H), 7.49 (t, *J* = 4.6 Hz, 1H), 7.36-7.38 (m, 2H), 7.30-7.32 (m, 1H), 7.13 (d, *J* = 3.9 Hz, 1H), 7.01 (s, 1H), 7.39 (d, *J* = 2.6 Hz, 1H), 2.62-2.65 (m, 1H), 1.75-1.79 (m, 2H), 1.60 (br s, 2H), 1.45-1.47 (m, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 179.1, 140.3, 133.2, 132.6, 130.7, 128.5, 128.1, 127.3, 122.9, 120.0, 110.5, 100.2, 75.6, 33.5, 30.7, 24.9; **IR** (ATR) ν = 2957, 2868, 1664, 1494, 1333, 1085 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{18}H_{18}NO$ 264.1383, found 264.1388.

1-(2-(Hex-1-ynyl)phenyl)-1*H*-pyrrole-2-carbaldehyde (5j). Colorless oil (78.5 mg, 77.3%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.46 (s, 1H), 7.50-7.52 (m, 1H), 7.36-7.38 (m, 2H), 7.29-7.31 (m, 1H), 7.12-7.13 (m, 1H), 7.03 (s, 1H), 7.40 (t, *J* = 3.1 Hz, 1H), 2.22 (t, *J* = 6.9 Hz, 2H), 1.35-1.38 (m, 2H), 1.22-1.28 (m, 2H), 0.84 (t, *J* = 7.3 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 179.1, 140.2, 133.2, 132.8, 130.8, 128.5, 128.2, 127.4, 122.7, 120.2, 110.5, 95.9, 76.1, 30.3, 21.8, 19.1, 13.6; **IR** (ATR) ν = 2932, 2862, 1665, 1494, 1333, 1085 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{17}H_{18}NO$ 252.1383, found 252.1398.

1-(5-Chloro-2-(phenylethynyl)phenyl)-1*H*-pyrrole-2-carbaldehyde (5k). Off white solid, mp: 130.0-130.8 °C (99.9 mg, 90.3%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.56 (s, 1H), 7.56 (d, *J* = 8.2 Hz, 1H), 7.40-7.43 (m, 2H), 7.23-7.30 (m, 5H), 7.17-7.18 (m, 1H), 7.08 (s, 1H), 6.47 (t, *J* = 3.1 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 178.7, 141.6, 134.4, 133.3, 131.6, 131.2, 129.0, 128.9, 128.4, 127.8, 122.4, 122.1, 120.7, 111.0, 94.96, 84.2; **IR** (ATR) ν = 3061, 2790, 1656, 1387, 1525, 1093 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{19}H_{13}ClNO$ 306.0680, found 306.0674.

1-(5-Chloro-2-((4-fluorophenyl)ethynyl)phenyl)-1*H*-pyrrole-2-carbaldehyde (5l). Off white solid; mp: 139.9-142.2 °C (100.7 mg, 86.2%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.55 (s, 1H), 7.54 (d, *J* = 8.2 Hz, 1H), 7.40-7.43 (m, 2H), 7.20-7.24 (m, 2H), 7.17 (dd, *J* = 1.2, 3.8 Hz, 1H), 7.08 (s, 1H), 6.97 (t, *J* = 8.7 Hz, 2H), 6.47 (t, *J* = 3.2 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 178.7, 162.9 (d, *J* = 249.0 Hz), 141.5, 134.5, 133.6 (d, *J* = 8.4 Hz), 133.3, 133.2, 131.2, 129.0, 127.9, 122.0, 120.5, 118.5 (d, *J* = 3.5 Hz), 115.8 (d, *J* = 22.1 Hz), 111.1, 93.9,

83.9; **IR** (ATR) ν = 2864, 2793, 1653, 1508, 1386, 1092 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{19}H_{12}ClFNO$ 324.0586, found 324.0592.

1-(5-Chloro-2-((4-methoxyphenyl)ethynyl)phenyl)-1*H*-pyrrole-2-carbaldehyde (5m). Off white solid; mp: 120.4-121.1 °C (84.3 mg, 83.2%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.55 (s, 1H), 7.53 (d, *J* = 8.2 Hz, 1H), 7.39-7.42 (m, 2H), 7.16-7.19 (m, 3H), 7.08 (s, 1H), 6.80 (d, *J* = 8.8 Hz, 2H), 6.46 (dd, *J* = 2.8, 3.8 Hz, 1H), 3.79 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 178.8, 160.2, 141.3, 133.98, 133.3, 133.1, 133.0, 131.2, 128.96, 127.8, 121.1, 114.4, 114.1, 110.98, 95.3, 83.0, 55.4; **IR** (ATR) ν = 3061, 2837, 1654, 1511, 1243, 1075 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{20}H_{15}ClNO_2$ 336.0781, found 336.0789.

1-(5-Chloro-2-(thiophen-3-ylethynyl)phenyl)-1*H*-pyrrole-2-carbaldehyde (5n). Brown solid; mp: 107.8-108.7 °C (65.3 mg, 69.4%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.55 (s, 1H), 7.53 (d, *J* = 8.3 Hz, 1H), 7.39-7.42 (m, 2H), 7.31 (s, 1H), 7.23 (d, *J* = 4.6 Hz, 1H), 7.16 (s, 1H), 7.07 (s, 1H), 6.94 (d, *J* = 4.6 Hz, 1H), 6.46 (s, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 178.7, 141.4, 134.3, 133.2, 133.1, 131.1, 129.59, 129.56, 128.9, 127.8, 125.6, 121.9, 121.4, 120.6, 111.0, 90.3, 83.8; **IR** (ATR) ν = 3099, 2862, 1653, 1524, 1386, 1075 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{17}H_{11}ClNOS$ 312.0244, found 312.0248.

1-(5-Chloro-2-(cyclohexenylethynyl)phenyl)-1*H*-pyrrole-2-carbaldehyde (5o). Yellow oil (80.7 mg, 72%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.50 (s, 1H), 7.44 (d, *J* = 8.2 Hz, 1H), 7.34-7.37 (m, 2H), 7.12-7.13 (m, 1H), 7.01 (s, 1H), 6.42 (t, *J* = 3.2 Hz, 1H), 5.98 (s, 1H), 2.06 (brs, 2H), 1.96 (brs, 2H), 1.56 (brs, 2H), 1.53 (brs, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 178.8,

141.1, 136.7, 133.7, 133.2, 130.9, 128.9, 127.7, 121.5, 121.2, 120.3, 110.9, 97.1, 81.6, 28.6, 25.9, 22.2, 21.4; **IR** (ATR) ν = 3110, 2927, 1665, 1490, 1362, 1096 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+Na]^+$ calcd for $C_{19}H_{16}ClNNaO$ 332.0813, found 332.0812.

1-(4-Methyl-2-(phenylethynyl)phenyl)-1*H*-pyrrole-2-carbaldehyde (5p). Brown solid, mp: 115.9-116.7 °C (84.6 mg, 92.2%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.52 (s, 1H), 7.46 (s, 1H), 7.23-7.27 (m, 7H), 7.17 (d, *J* = 2.6 Hz, 1H), 7.08 (s, 1H), 6.44 (t, *J* = 3.1 Hz, 1H), 2.43 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 179.1, 138.7, 137.9, 133.4, 133.0, 131.6, 131.3, 129.8, 128.6, 128.4, 127.3, 122.7, 121.7, 120.7, 110.6, 93.8, 85.1, 21.1; **IR** (ATR) ν = 3103, 2975, 1653, 1504, 1389, 1188 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{20}H_{16}NO$ 286.1226, found 286.1231.

1-(2-((4-Fluorophenyl)ethynyl)-4-methylphenyl)-1*H*-pyrrole-2-carbaldehyde (5q). Off white solid; mp: 90.7-91.9 °C (95.9 mg, 82%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.51 (s, 1H), 7.44 (s, 1H), 7.17-7.25 (m, 5H), 7.06 (s, 1H), 6.96 (t, *J* = 7.9 Hz, 2H), 6.44 (s, 1H), 2.42 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 179.1, 162.7 (d, *J* = 248.7 Hz), 138.8, 137.9, 133.5 (d, *J* = 8.4 Hz), 133.4, 132.9, 131.3, 129.9, 127.3, 121.5, 120.6, 118.8, 115.7 (d, *J* = 22.0 Hz), 110.6, 92.7, 84.9, 21.1; **IR** (ATR) ν = 3109, 2793, 1660, 1508, 1224, 1083 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{20}H_{15}FNO$ 304.1132, found 304.1150.

1-(2-((4-Methoxyphenyl)ethynyl)-4-methylphenyl)-1*H*-pyrrole-2-carbaldehyde (5r). Off white solid; mp: 86.9-87.8 °C (101.7 mg, 83.6%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.51 (s, 1H), 7.43 (s, 1H), 7.25 (s, 1H), 7.17-7.22 (m, 4H), 7.08 (s, 1H), 7.79 (d, *J* = 8.4 Hz, 2H), 6.44 (s,

1H), 3.79 (s, 3H), 2.42 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 179.2, 159.9, 138.7, 137.6, 133.4, 133.1, 132.8, 131.2, 129.4, 127.2, 122.0, 120.4, 114.8, 114.0, 110.5, 94.0, 83.9, 55.4, 21.1; **IR** (ATR) ν = 3098, 2870, 1663, 1512, 1387, 1027 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+Na]^+$ calcd for $C_{21}H_{17}NNaO_2$ 338.1151, found 338.1142.

1-(4-Methyl-2-(thiophen-3-ylethynyl)phenyl)-1*H*-pyrrole-2-carbaldehyde (5s). Brown solid; mp: 113.9-114.6 °C (100.6 mg, 89.5%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.52 (s, 1H), 7.44 (s, 1H), 7.31 (d, *J* = 2.6 Hz, 1H), 7.21-7.28 (m, 3H), 7.16-7.17 (m, 1H), 7.07 (s, 1H), 6.95 (d, *J* = 4.9 Hz, 1H), 6.43 (t, *J* = 3.2 Hz, 1H), 2.43 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 179.2, 138.7, 137.9, 133.4, 132.9, 131.3, 129.72, 129.70, 129.2, 127.3, 125.5, 121.8, 121.6, 120.4, 110.6, 89.1, 84.8, 21.2; **IR** (ATR) ν = 3111, 2861, 1649, 1526, 1332, 1087 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{18}H_{14}NOS$ 292.0791, found 292.0798.

1-(2-(Cyclohexenylethynyl)-4-methylphenyl)-1*H*-pyrrole-2-carbaldehyde (5t). Colorless oil (95.1 mg, 85.2%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.46 (s, 1H), 7.34 (s, 1H), 7.16-7.25 (m, 2H), 7.13 (dd, *J* = 1.4, 3.9 Hz, 1H), 7.01 (d, *J* = 1.6 Hz, 1H), 6.39 (dd, *J* = 2.7, 3.8 Hz, 1H), 5.96-5.98 (m, 1H), 2.39 (s, 3H), 2.05-2.06 (m, 2H), 1.96-1.97 (m, 2H), 1.53-1.56 (m, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 179.2, 139.96, 138.6, 136.1, 133.3, 132.9, 131.0, 129.8, 129.2, 127.2, 122.1, 120.4, 110.4, 95.9, 82.5, 28.6, 25.8, 22.2, 21.5, 21.1; **IR** (ATR) ν = 3111, 2925, 1667, 1502, 1333, 1081 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{20}H_{20}NO$ 290.1539, found 290.1547.

Methyl 4-(2-formyl-1*H*-pyrrol-1-yl)-3-(phenylethynyl)benzoate (5u). Off white solid, mp:

81.6-82.9 °C (85 mg, 83.3%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.56 (s, 1H), 8.32 (s, 1H), 8.09 (d, *J* = 8.2 Hz, 1H), 7.44 (d, *J* = 8.3 Hz, 1H), 7.29-7.30 (m, 5H), 7.19 (d, *J* = 2.8 Hz, 1H), 7.14 (s, 1H), 6.49 (t, *J* = 3.0 Hz, 1H), 3.97 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 178.7, 165.7, 144.1, 134.0, 133.2, 131.7, 131.3, 130.4, 129.9, 129.0, 128.5, 127.6, 122.4, 122.3, 122.2, 111.1, 94.9, 84.4, 52.7; **IR** (ATR) ν = 3121, 2870, 1723, 1656, 1429, 1250, 1107 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{21}H_{16}NO_3$ 330.1125, found 330.1135.

Methyl 4-(2-formyl-1*H*-pyrrol-1-yl)-3-((4-methoxyphenyl)ethynyl)benzoate (5v). Off white solid; mp: 138.0-138.9 °C (90 mg, 85.7%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.55 (s, 1H), 8.29 (s, 1H), 8.06 (d, *J* = 8.2 Hz, 1H), 7.43 (d, *J* = 8.2 Hz, 1H), 7.19-7.23 (m, 3H), 7.13 (s, 1H), 6.81 (d, *J* = 8.5 Hz, 2H), 6.48 (s, 1H), 3.97(s, 3H), 3.80 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 178.7, 165.8, 160.2, 143.8, 133.7, 133.2, 131.2, 130.3, 129.5, 127.5, 122.5, 122.1, 114.3, 114.1, 111.0, 95.2, 83.2, 55.4, 52.6; **IR** (ATR) ν = 3001, 2836, 1713, 1660, 1513, 1244, 1100 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{22}H_{18}NO_4$ 360.1230, found 360.1237.

1-(4-Nitro-2-(phenylethynyl)phenyl)-1*H*-pyrrole-2-carbaldehyde (5w). Brown solid, mp: 165.5-166.7 °C (91.2 mg, 82.2%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.59 (s, 1H), 8.48 (s, 1H), 8.26 (d, *J* = 7.6 Hz, 1H), 7.53 (d, *J* = 8.2 Hz, 1H), 7.26-7.30 (m, 5H), 7.21 (s, 1H), 7.17 (s, 1H), 6.54 (s, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 178.5, 147.3, 145.8, 133.1, 131.8, 131.4, 129.5, 128.6, 128.5, 127.6, 124.1, 123.5, 123.3, 121.7, 111.5, 96.4, 83.4; **IR** (ATR) ν = 3080, 2843, 1657, 1519, 1342, 1071 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{19}H_{13}N_2O_3$ 317.0921, found 317.0915.

1-(4-Nitro-2-(m-tolylethynyl)phenyl)-1*H*-pyrrole-2-carbaldehyde (5x). Yellow solid; mp: 143.2-144.8 °C (77.2 mg, 80%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.59 (s, 1H), 8.48 (d, *J* = 2.5 Hz, 1H), 8.26 (dd, *J* = 2.5, 8.7 Hz, 1H), 7.52 (d, *J* = 8.7 Hz, 1H), 7.17-7.22 (m, 4H), 7.08-7.12 (m, 2H), 6.53 (t, *J* = 3.3 Hz, 1H), 2.32 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 178.5, 147.2, 145.7, 138.3, 133.1, 132.3, 131.4, 130.4, 128.9, 128.48, 128.46, 127.7, 124.1, 123.4, 121.5, 111.5, 96.7, 83.0, 21.3; **IR** (ATR) ν = 3082, 2829, 1668, 1518, 1343, 1093 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{20}H_{15}N_2O_3$ 331.1077, found 331.1086.

Representative Procedure for the Synthesis of 6

Condition A: In a vial containing **5a** (27 mg, 0.1 mmol) was added TFA (0.5 mL) and the resulting solution was stirred at 90 °C for 1 h. The reaction mixture was cooled down to rt and concentrated *in vacuo* to yield the crude product. Purification by flash chromatography on silica gel (hexanes: EtOAc, 95:5) gave **6a** as a yellow solid (26.7 mg, 99%).

Condition B: In a vial containing **5d** (30 mg, 0.105 mmol) was added DCE (0.5 mL) and TFA (0.5 mL) and the resulting solution was stirred at 90 °C for 1 h. The reaction mixture was cooled down to rt and concentrated *in vacuo* to yield the crude product. Purification by flash chromatography on silica gel (hexanes: EtOAc, 95:5) gave **6d** as a yellow solid (24.6 mg, 82%).

Phenyl(pyrrolo[1,2-*a*]quinolin-5-yl)methanone (6a). Yellow solid, mp: 94.4-95.2 °C (26.7 mg, 99%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.36 (d, *J* = 8.1 Hz, 1H), 7.95-7.99 (m, 2H), 7.91 (d, *J* = 7.3 Hz, 2H), 7.56-7.63 (m, 3H), 7.50 (t, *J* = 7.6 Hz, 2H), 7.38 (t, *J* = 7.5 Hz, 1H), 6.88 (t, *J* = 3.3 Hz, 1H), 6.73 (d, *J* = 3.2 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 196.3, 139.0, 133.2, 132.8, 130.3, 128.7, 128.61, 128.58, 127.9, 125.9, 125.2, 124.4, 121.5, 114.7, 114.5, 114.3, 107.9; **IR** (ATR) ν = 3060, 2925, 1639, 1593, 1260, 1229, 1083 cm^{-1}; **HRMS** (ESI-

QTOF) *m/z* $[M+H]^+$ calcd for $C_{19}H_{14}NO$ 272.1070, found 272.1069.

(4-Fluorophenyl)(pyrrolo[1,2-*a*]quinolin-5-yl)methanone (6b). Yellow solid; mp: 124.8-125.9 °C (55.6 mg, 92.7%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.29 (dd, *J* = 0.9, 8.2 Hz, 1H), 7.93-7.99 (m, 4H), 7.55-7.59 (m, 2H), 7.36-7.40 (m, 1H), 7.17 (t, *J* = 8.6 Hz, 2H), 6.88 (dd, *J* = 3.0, 3.7 Hz, 1H), 6.74 (dd, *J* = 1.0, 3.8 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 194.7, 165.7 (d, *J* = 253.0 Hz), 135.2 (d, *J* = 3.0 Hz), 133.2, 132.8 (d, *J* = 9.1 Hz), 128.7, 128.6, 127.7, 125.7, 124.7, 124.4, 121.3, 115.8, 115.6, 114.7, 114.5 (d, *J* = 16.7 Hz), 107.9; **IR** (ATR) ν = 3067, 2892, 1638, 1592, 1449, 1092 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{19}H_{13}FNO$ 290.0976, found 290.0982.

(3-Fluorophenyl)(pyrrolo[1,2-*a*]quinolin-5-yl)methanone (6c). Yellow solid; mp: 126.7-128.2 °C (41.4 mg, 82.8%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.38 (d, *J* = 8.2 Hz, 1H), 8.00 (s, 1H), 7.96 (d, *J* = 8.4 Hz, 1H), 7.66 (d, *J* = 7.7 Hz, 1H), 7.57-7.61 (m, 3H), 7.44-7.50 (m, 1H), 7.40 (t, *J* = 7.7 Hz, 1H), 7.31 (dt, *J* = 1.8, 8.3 Hz, 1H), 6.89 (t, *J* = 3.3 Hz, 1H), 6.77 (d, *J* = 3.6 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 194.7, 162.7 (d, *J* = 247.0 Hz), 141.2, 133.2, 130.2 (d, *J* = 7.7 Hz), 128.7, 128.6, 127.8, 126.0 (d, *J* = 3.0 Hz), 125.6, 125.1, 124.5, 121.2, 119.7 (d, *J* = 21.3 Hz), 116.9 (d, *J* = 22.1 Hz), 115.0, 114.6, 114.5, 108.5; **IR** (ATR) ν = 2948, 2835, 1649, 1450, 1265, 1114 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{19}H_{13}FNO$ 290.0976, found 290.0975.

Pyrrolo[1,2-*a*]quinolin-5-yl(*m*-tolyl)methanone (6d). Yellow solid; mp: 107.9-108.6 °C (24.6 mg, 82%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.35 (d, *J* = 8.2 Hz, 1H), 7.95-7.99 (m, 2H),

7.74 (s, 1H), 7.68 (d, J = 7.4 Hz, 1H), 7.56-7.60 (m, 2H), 7.36-7.44 (m, 3H), 6.88 (t, J = 3.0 Hz, 1H), 6.73 (d, J = 3.5 Hz, 1H), 2.43 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 196.5, 139.0, 138.4, 133.6, 133.2, 130.6, 128.7, 128.6, 128.4, 127.8, 127.6, 126.1, 124.98, 124.4, 121.5, 114.6, 114.5, 114.3, 107.8, 21.5; **IR** (ATR) ν = 3137, 2921, 1634, 1448, 1267, 1095 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{20}H_{16}NO$ 286.1226, found 286.1236.

(4-Methoxyphenyl)(pyrrolo[1,2-*a*]quinolin-5-yl)methanone (6e). Yellow gum (25.2 mg, 84%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.18 (dd, J = 0.8, 8.2 Hz, 1H), 7.91-7.97 (m, 4H), 7.54-7.58 (m, 2H), 7.33-7.37 (m, 1H), 6.97 (d, J = 8.8 Hz, 2H), 6.87 (dd, J = 3.0, 3.6 Hz, 1H), 6.71 (dd, J = 1.0, 3.8 Hz, 1H), 3.90 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 195.0, 163.7, 133.2, 132.7, 131.4, 128.9, 128.5, 127.8, 126.6, 124.2, 123.5, 121.6, 114.5, 114.3, 114.1, 113.8, 107.1, 55.7; **IR** (ATR) ν = 3002, 2837, 1638, 1592, 1252, 1093 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{20}H_{16}NO_2$ 302.1176, found 302.1184.

Pyrrolo[1,2-*a*]quinolin-5-yl(thiophen-3-yl)methanone (6f). Yellow solid; mp: 119.2-120.9 °C (32.4 mg, 81%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.32 (d, J = 8.2 Hz, 1H), 7.93-7.97 (m, 3H), 7.74 (s, 1H), 7.66 (d, J = 5.0 Hz, 1H), 7.56 (t, J = 7.7 Hz, 1H), 7.35-7.41 (m, 2H), 6.88 (t, J = 3.3 Hz, 1H), 6.75 (d, J = 3.6 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 189.4, 142.96, 134.1, 133.2, 128.7, 128.6, 127.6, 126.8, 126.5, 124.3, 123.9, 121.1, 114.6, 114.5, 114.3, 107.7; **IR** (ATR) ν = 3137, 2892, 1634, 1447, 1262, 1160 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{17}H_{12}NOS$ 278.0634, found 278.0629.

(6-Methoxynaphthalen-2-yl)(pyrrolo[1,2-*a*]quinolin-5-yl)methanone (6g). Yellow solid;

mp: 185.8-186.4 °C (34.8, 87%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.28-8.31 (m, 2H), 8.05 (d, *J* = 8.4 Hz, 1H), 7.96-7.99 (m, 2H), 7.84 (d, *J* = 8.6 Hz, 1H), 7.78 (d, *J* = 9.6 Hz, 1H), 7.65 (s, 1H), 7.58 (t, *J* = 7.7 Hz, 1H), 7.37 (t, *J* = 7.6 Hz, 1H), 7.19-7.21 (m, 2H), 6.89 (t, *J* = 3.0 Hz, 1H), 6.72 (d, *J* = 3.3 Hz, 1H), 3.97 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 196.0, 159.9, 137.3, 134.0, 133.2, 132.1, 131.2, 128.8, 128.6, 127.8, 127.3, 126.5, 124.3, 124.2, 121.6, 119.8, 114.5, 114.4, 114.2, 107.5, 105.9, 55.6; **IR** (ATR) ν = 3062, 2848, 1648, 1616, 1271, 1093 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{24}H_{18}NO_2$ 352.1332, found 352.1336.

Cyclohexenyl(pyrrolo[1,2-*a*]quinolin-5-yl)methanone (6h). Yellow gum (9.8 mg, 32.6%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.99 (d, *J* = 8.1 Hz, 1H), 7.91-7.92 (m, 2H), 7.53 (t, *J* = 7.2 Hz, 1H), 7.45 (s, 1H), 7.33 (t, *J* = 7.5 Hz, 1H), 6.84 (t, *J* = 3.2 Hz, 1H), 6.77 (s, 1H), 6.68 (d, *J* = 2.8 Hz, 1H), 2.50 (br s, 2H), 2.25 (br s, 2H), 1.77-1.79 (m, 2H), 1.68-1.71 (m, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 197.8, 144.8, 140.5, 133.3, 129.0, 128.4, 127.5, 127.2, 124.1, 121.8, 121.7, 114.5, 113.9, 113.7, 106.2, 26.4, 23.8, 22.2, 21.8; **IR** (ATR) ν = 2928, 2857, 1626, 1553, 1449, 1092 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{19}H_{18}NO$ 276.1383, found 276.1392.

(8-Chloropyrrolo[1,2-*a*]quinolin-5-yl)(phenyl)methanone (6i). Yellow solid, mp: 158.7-159.8 °C (33.4 mg, 83.5%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.34 (d, *J* = 8.8 Hz, 1H), 7.87-7.94 (m, 4H), 7.60-7.62 (m, 2H), 7.50 (t, *J* = 7.2 Hz, 2H), 7.34 (d, *J* = 8.6 Hz, 1H), 6.89 (s, 1H), 6.75 (s, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 195.9, 138.8, 134.3, 133.9, 132.9, 130.2, 129.2, 128.8, 128.6, 125.6, 125.1, 124.8, 119.96, 115.0. 114.9, 114.6, 108.6; **IR** (ATR) ν = 3144, 3036, 1636, 1590, 1423, 1096 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for

$C_{19}H_{13}ClNO$ 306.0680, found 306.0684.

(8-Chloropyrrolo[1,2-*a*]quinolin-5-yl)(4-fluorophenyl)methanone (6j). Yellow solid; mp: 194.0-195.2 °C (30.8 mg, 77%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.28 (d, *J* = 8.8 Hz, 1H), 7.90-7.94 (m, 4H), 7.57 (s, 1H), 7.34 (d, *J* = 8.8 Hz, 1H), 7.18 (t, *J* = 8.5 Hz, 2H), 6.90 (t, *J* = 3.3 Hz, 1H), 6.76 (d, *J* = 3.8 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 194.3, 165.7 (d, *J* = 253.3 Hz), 135.0 (d, *J* = 2.9 Hz), 134.4, 133.9, 132.8 (d, *J* = 9.2 Hz), 129.1, 128.7, 125.1, 125.0, 124.8, 119.8, 115.8 (d, *J* = 21.8 Hz), 115.1, 115.0, 114.7, 108.6; **IR** (ATR) ν = 3069, 2983, 1644, 1593, 1230, 1096 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{19}H_{12}ClFNO$ 324.0586, found 324.0585.

(8-Chloropyrrolo[1,2-*a*]quinolin-5-yl)(4-methoxyphenyl)methanone (6k). Yellow solid; mp: 180.4-182.1 °C (17.2 mg, 86%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.16 (d, *J* = 8.8 Hz, 1H), 7.89-7.93 (m, 4H), 7.55 (s, 1H), 7.31 (dd, *J* = 1.8, 8.9 Hz, 1H), 6.97 (d, *J* = 8.8 Hz, 2H), 6.88 (t, *J* = 3.3 Hz, 1H), 6.72 (d, *J* = 3.4 Hz, 1H), 3.90 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 194.6, 163.7, 134.2, 133.97, 132.6, 131.2, 129.2, 128.98, 125.9, 124.6, 123.9, 120.1, 114.7, 114.6, 114.5, 113.9, 107.8, 55.7; **IR** (ATR) ν = 2920, 2845, 1635, 1599, 1251, 1097 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+Na]^+$ calcd for $C_{20}H_{14}ClNNaO_2$ 358.0605, found 358.0602.

(8-Chloropyrrolo[1,2-*a*]quinolin-5-yl)(thiophen-3-yl)methanone (6l). Yellow solid; mp: 178.9-179.8 °C (25.2 mg, 84%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.29 (d, *J* = 8.8 Hz, 1H), 7.97 (d, *J* = 1.8 Hz, 1H), 7.91 (dd, *J* = 1.7, 9.0 Hz, 2H), 7.75 (s, 1H), 7.65 (d, *J* = 5.0 Hz, 1H), 7.41 (dd, *J* = 3.0, 5.0 Hz, 1H), 7.32 (dd, *J* = 1.8, 8.8 Hz, 1H), 6.89 (t, *J* = 3.3 Hz, 1H), 6.77 (d,

J = 3.6 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 189.1, 142.7, 134.4, 134.1, 133.9, 129.1, 128.8, 128.6, 126.7, 126.1, 124.7, 124.2, 119.6, 114.9, 114.6, 108.3; **IR** (ATR) ν = 3112, 2917, 1629, 1430, 1265, 1093 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{17}H_{11}ClNOS$ 312.0244, found 312.0249.

(8-Chloropyrrolo[1,2-*a*]quinolin-5-yl)(cyclohexenyl)methanone (6m). Yellow solid; mp: 166.1-167.2 °C (10.4 mg, 34.6%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 8.4 Hz, 1H), 7.89 (s, 1H), 7.84 (s, 1H), 7.46 (s, 1H), 7.29 (d, *J* = 8.8 Hz, 1H), 6.86 (s, 1H), 6.75 (s, 1H), 6.70 (d, *J* = 3.6 Hz, 1H), 2.48 (br s, 2H), 2.26 (br s, 2H), 1.76-1.77 (m, 2H), 1.69-1.70 (m, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 197.4, 144.9, 140.4, 134.1, 134.0, 129.1, 128.9, 126.4, 124.5, 122.2, 120.2, 114.6, 114.5, 114.0, 106.9, 26.4, 23.8, 22.1, 21.8; **IR** (ATR) ν = 3107, 2796, 1650, 1524, 1385, 1075 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{19}H_{17}ClNO$ 310.0993, found 310.0997.

(7-Methylpyrrolo[1,2-*a*]quinolin-5-yl)(phenyl)methanone (6n). Yellow gum (34.5 mg, 86.2%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.17 (s, 1H), 7.95 (s, 1H), 7.91 (d, *J* = 7.4 Hz, 2H), 7.85 (d, *J* = 8.5 Hz, 1H), 7.61 (t, *J* = 7.3 Hz, 1H), 7.56 (s, 1H), 7.50 (t, *J* = 7.6 Hz, 2H), 7.39 (d, *J* = 8.5 Hz, 1H), 6.85 (t, *J* = 3.3 Hz, 1H), 6.70 (d, *J* = 3.6 Hz, 1H), 2.45 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 196.8, 138.9, 134.1, 132.9, 131.3, 130.4, 129.8, 128.6, 128.5, 127.5, 125.6, 125.4, 121.3, 114.6, 114.4, 114.1, 107.8, 21.4; **IR** (ATR) ν = 2920, 2855, 1639, 1595, 1426, 1231, 1092 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{20}H_{16}NO$ 286.1226, found 286.1245.

(4-Fluorophenyl)(7-methylpyrrolo[1,2-*a*]quinolin-5-yl)methanone (6o). Yellow solid; mp: 117.2-118.6 °C (34 mg, 89.5%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.08 (s, 1H), 7.93-7.97 (m, 3H), 7.86 (d, *J* = 8.5 Hz, 1H), 7.53 (s, 1H), 7.40 (d, *J* = 8.4 Hz, 1H), 7.17 (t, *J* = 8.6 Hz, 2H), 6.86 (t, *J* = 3.3 Hz, 1H), 6.72 (d, *J* = 3.6 Hz, 1H), 2.45 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 194.8, 165.7 (d, *J* = 252.7 Hz), 135.2 (d, *J* = 2.9 Hz), 134.0, 132.8 (d, *J* = 9.1 Hz), 131.2, 129.8, 128.4, 127.4, 125.5, 124.6, 121.2, 115.7 (d, *J* = 21.5 Hz), 114.5, 114.4, 114.1, 107.6, 21.4; **IR** (ATR) ν = 3039, 2922, 1641, 1593, 1261, 1089 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{20}H_{15}FNO$ 304.1132, found 304.1140.

(4-Methoxyphenyl)(7-methylpyrrolo[1,2-*a*]quinolin-5-yl)methanone (6p). Yellow solid; mp: 106.3-107.7 °C (24.8 mg, 82.7%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.94-7.99 (m, 4H), 7.85 (d, *J* = 8.6 Hz, 1H), 7.51 (m, 1H), 7.38 (d, *J* = 8.8 Hz, 1H), 6.97 (d, *J* = 8.2 Hz, 2H), 6.84 (s, 1H), 6.68 (s, 1H), 3.90 (s, 3H), 2.43 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 195.1, 163.7, 133.8, 132.7, 131.4, 131.3, 129.7, 128.7, 127.4, 126.4, 123.4, 121.5, 114.4, 114.0, 113.8, 106.8, 55.7, 21.4; **IR** (ATR) ν = 3070, 2862, 1653, 1524, 1386, 1075 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{21}H_{18}NO_2$ 316.1332, found 316.1348.

(7-Methylpyrrolo[1,2-*a*]quinolin-5-yl)(thiophen-3-yl)methanone (6q). Yellow gum (29.6 mg, 84.6%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.11 (s, 1H), 7.98 (t, *J* = 1.4 Hz, 1H), 7.94 (s, 1H), 7.84 (d, *J* = 8.5 Hz, 1H), 7.71 (s, 1H), 7.67 (dd, *J* = 0.7, 5.0 Hz, 1H), 7.37-7.42 (m, 2H), 6.85 (t, *J* = 3.3 Hz, 1H), 6.73 (d, *J* = 3.0 Hz, 1H), 2.45 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 189.6, 143.1, 134.1, 133.98, 131.3, 129.8, 128.6, 128.5, 127.3, 126.7, 126.5, 123.8, 120.98, 114.4, 114.0, 107.4, 21.4; **IR** (ATR) ν = 3102, 2920, 1630, 1426, 1260, 1091 cm^{-1}; **HRMS**

(ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{18}H_{14}NOS$ 292.0791, found 292.0798.

Cyclohexenyl(7-methylpyrrolo[1,2-*a*]quinolin-5-yl)methanone (6r). Yellow gum (16.3 mg, 34%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.87 (s, 1H), 7.78-7.81 (m, 2H), 7.42 (s, 1H), 7.35 (dd, *J* = 1.2, 8.5 Hz, 1H), 6.81 (t, *J* = 3.3 Hz, 1H), 6.78 (t, *J* = 3.8 Hz, 1H), 6.66 (d, *J* = 2.8 Hz, 1H), 2.50 (br s, 2H), 2.43 (s, 3H), 2.25-2.27 (m, 2H), 1.75-1.81 (m, 2H), 1.68-1.72 (m, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 197.98, 144.8, 140.5, 133.7, 131.4, 129.6, 128.8, 127.1, 126.9, 121.8, 121.5, 114.3, 113.6, 113.5, 105.97, 26.4, 23.8, 22.2, 21.8, 21.4; **IR** (ATR) ν = 2924, 2857, 1628, 1429, 1219, 1090 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{20}H_{20}NO$ 290.1539, found 290.1549.

Methyl 5-benzoylpyrrolo[1,2-*a*]quinoline-7-carboxylate (6s). Yellow solid, mp: 103.9-105.2 °C (26.4 mg, 88%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.08 (s, 1H), 8.24 (d, *J* = 8.6 Hz, 1H), 7.98-8.01 (m, 2H), 7.92 (d, *J* = 7.6 Hz, 2H), 7.61-7.64 (m, 2H), 7.51 (t, *J* = 7.6 Hz, 2H), 6.92 (t, *J* = 3.1 Hz, 1H), 6.77 (d, *J* = 3.6 Hz, 1H), 3.93 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 194.8, 165.7, 137.7, 134.98, 132.0, 129.3, 129.0, 128.6, 127.9, 127.7, 125.1, 124.7, 120.1, 114.4, 114.3, 113.7, 107.9, 51.4; **IR** (ATR) ν = 2924, 2862, 1705, 1625, 1431, 1220, 1092 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{21}H_{16}NO_3$ 330.1125, found 330.1129.

Methyl 5-(4-methoxybenzoyl)pyrrolo[1,2-*a*]quinoline-7-carboxylate (6t). Yellow solid, mp: 177.2-178.6 °C (24.6 mg, 82%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.92 (s, 1H), 8.23 (d, *J* = 8.8 Hz, 1H), 7.97-7.99 (m, 2H), 7.93 (d, *J* = 8.3 Hz, 2H), 7.58 (s, 1H), 6.98 (d, *J* = 8.4 Hz, 2H), 6.91 (s, 1H), 6.74 (s, 1H), 3.92 (s, 3H), 3.90 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ

194.4, 166.7, 163.8, 136.0, 132.7, 131.1, 129.9, 129.5, 129.1, 126.5, 125.98, 124.2, 121.2, 115.1, 114.96, 114.7, 113.9, 108.1, 55.7, 52.4; **IR** (ATR) ν = 3004, 2843, 1711, 1638, 1596, 1255, 1166 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{22}H_{18}NO_4$ 360.1230, found 360.1236.

(7-Nitropyrrolo[1,2-*a*]quinolin-5-yl)(phenyl)methanone (6u). Yellow solid, mp: 230.1-230.9 °C (17.2 mg, 86%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.40 (d, *J* = 2.4 Hz, 1H), 8.42 (dd, *J* = 2.5, 9.2 Hz, 1H), 8.03-8.06 (m, 2H), 7.91 (d, *J* = 7.7 Hz, 2H), 7.74 (s, 1H), 7.65 (t, *J* = 7.4 Hz, 1H), 7.53 (t, *J* = 7.6 Hz, 2H), 6.99 (t, *J* = 3.3 Hz, 1H), 6.85 (d, *J* = 3.8 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 195.2, 144.1, 138.3, 136.8, 133.2, 130.2, 129.0, 128.8, 127.2, 124.9, 124.3, 123.4, 121.6, 116.3, 116.1, 115.3, 110.1; **IR** (ATR) ν = 2921, 2852, 1636, 1511, 1331, 1262, 1090 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{19}H_{13}N_2O_3$ 317.0921, found 317.0916.

(7-Nitropyrrolo[1,2-*a*]quinolin-5-yl)(m-tolyl)methanone (6v). Yellow solid, mp: 191.8-192.9 °C (26.5 mg, 88.2%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.37 (s, 1H), 8.42 (d, *J* = 9.0 Hz, 1H), 8.03-8.05 (m, 2H), 7.73 (s, 2H), 7.67 (d, *J* = 7.4 Hz, 1H), 7.46 (d, *J* = 7.5 Hz, 1H), 7.40 (t, *J* = 7.5 Hz, 1H), 6.99 (s, 1H), 6.85 (d, *J* = 3.4 Hz, 1H), 2.45 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 195.4, 144.1, 138.7, 138.3, 136.7, 134.0, 130.6, 129.0, 128.6, 127.5, 126.9, 125.1, 124.3, 123.3, 121.6, 116.2, 116.1, 115.3, 110.0, 21.5; **IR** (ATR) ν = 3149, 2924, 1641, 1511, 1330, 1262, 1091 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{20}H_{15}N_2O_3$ 331.1077, found 331.1085.

7 and **8** were prepared by following the similar procedures for **3a** and **4a**, respectively.

1-(2-Bromo-4-methylphenyl)-1*H*-pyrrole (7). Brown oil (621.8 mg, 98%), **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.53 (s, 1H), 7.24 (d, *J* = 8.0 Hz, 1H), 7.18 (d, *J* = 8.1 Hz, 1H), 6.86 (t, *J* = 2.1 Hz, 2H), 6.34 (t, *J* = 2.1 Hz, 2H), 2.40 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 139.3, 138.0, 134.1, 128.9, 128.0, 122.4, 119.7, 109.0, 20.8; **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{11}H_{11}BrN$ 236.0069, found 236.0077.

1-(2-Bromo-4-methylphenyl)-1*H*-pyrrole-2-carbaldehyde (8). White solid, mp: 116.7-117.5 °C (198.5 mg, 71%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.48 (s, 1H), 7.51 (s, 1H), 7.19-7.24 (m, 2H), 7.12 (d, *J* = 3.5 Hz, 1H), 6.93 (s, 1H), 6.43 (t, *J* = 2.9 Hz, 1H), 2.41 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 178.7, 140.8, 136.1, 133.7, 133.0, 131.1, 128.9, 128.7, 121.9, 121.7, 110.8, 21.1; **IR** (ATR) ν = 3106, 2797, 1656, 1499, 1356, 1101 cm^{-1}; **HRMS** (ESI-QTOF) *m/z* $[M+H]^+$ calcd for $C_{12}H_{11}BrNO$ 264.0019, found 264.0032.

Acknowledgements

This work was supported by the National Research Foundation of Korea (NRF) grant funded by the Korea government (MSIP) (2014R1A2A1A11050491).

Supporting Information

^{1}H and ^{13}C NMR spectra of **3-8**.

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[12] **4b-4e** were prepared by following the similar procedure for **4a** except for the synthesis of **3e**. See the Experimental Section for details.