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Copper-Catalyzed Tandem Synthesis of Indolo-, Pyrrolo[2,1-*a*]isoquinolines, Naphthyridines and Bisindolo/Pyrrolo[2,1-*a*]isoquinolines via Hydroamination of *ortho*-Haloarylalkynes Followed by C-2 Arylation

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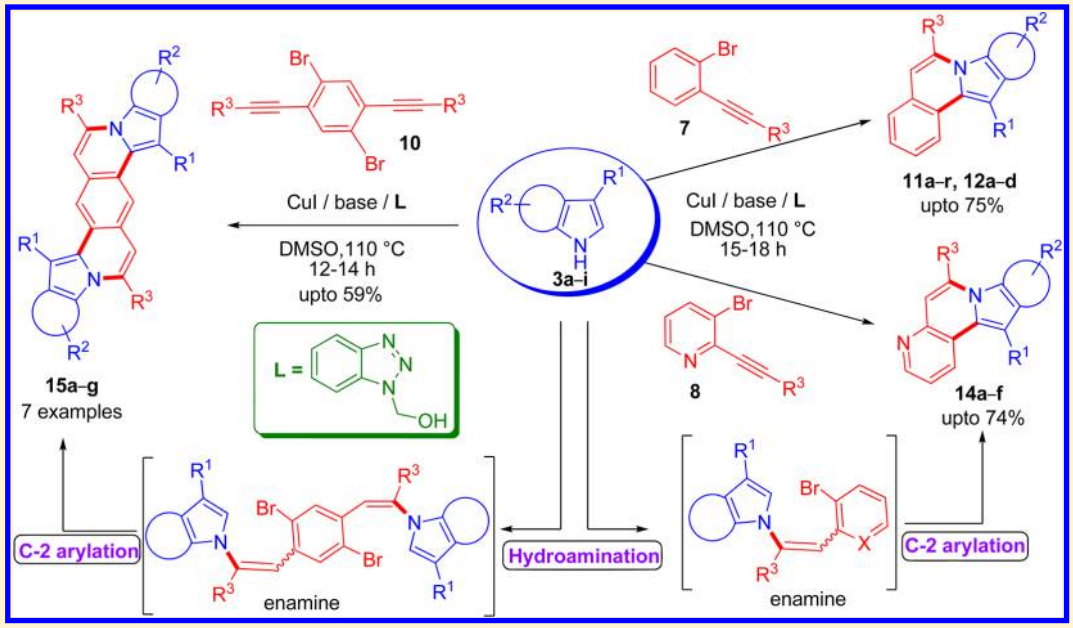
Supporting Information



ABSTRACT: An efficient approach for the copper-catalyzed regioselective tandem synthesis of diversely substituted indolo[2,1-*a*]isoquinolines **11a−r**, pyrrolo[2,1-*a*]isoquinolines **12a−d**, and indolo-, pyrrolo[2,1-*f*][1,6]naphthyridines **14a−f** via preferential addition of the heterocyclic amines onto the *ortho*-haloarylalkynes over *N*-arylation followed by intramolecular C-2 arylation is described. The scope of the developed chemistry was successfully extended for the direct synthesis of bisindolo-, pyrrolo[2,1-*a*]isoquinolines **15a−g**, a regioisomer of the bisindolo[1,2-*a*]quinolines used as organic single-crystal field-effect transistor. Hydroxymethyl benzotriazole, which is an inexpensive and air stable compound, has been used as a ligand to carry out this one-step conversion of simple, readily available starting materials into an interesting class of heterocyclic compounds.

INTRODUCTION

Development of new approaches for the synthesis of heterocycles, carbocyclic and natural-product-like compound, employing efficient and atom-economical routes, is currently a popular research area. In recent years, transition metal-catalyzed tandem reactions have emerged as a useful tool for the synthesis of multiring heterocyclic compounds,[1] because of the intriguing selectivity, high atom economy,[2] and exceptional ability to activate π-systems, especially alkynes, toward intermolecular and intramolecular nucleophilic attack.[3] Among the transition-metal-catalyzed organic transformations, copper and palladium are extensively used due to their low toxicity and tolerance of many important functional groups.[4] Copper-catalyzed reactions have received significant interest in the past two decades due to their effectiveness and low cost.[3f,5,6] The reported annulation chemistry for the synthesis of heterocycles from alkynes proceeds through π-complexation of the alkyne, followed by attack of the resulting η^2-metal complex by the appropriate adjacent functionalized arene.[3a,7]

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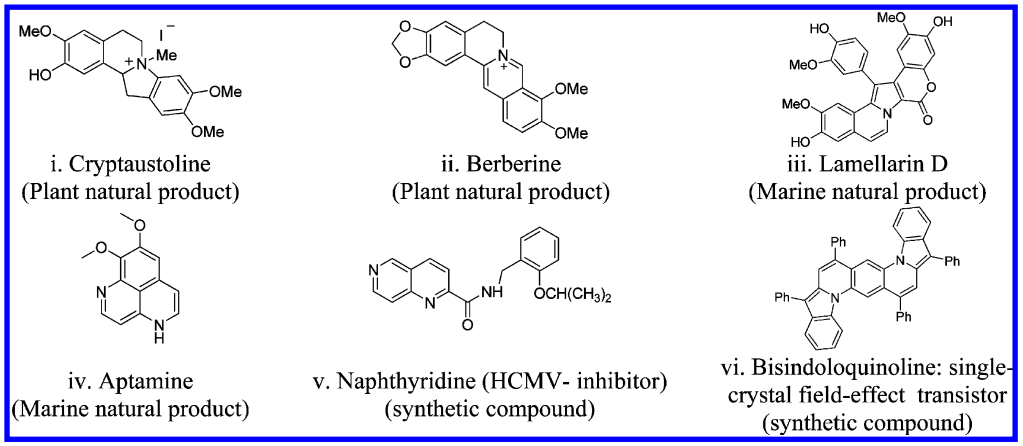
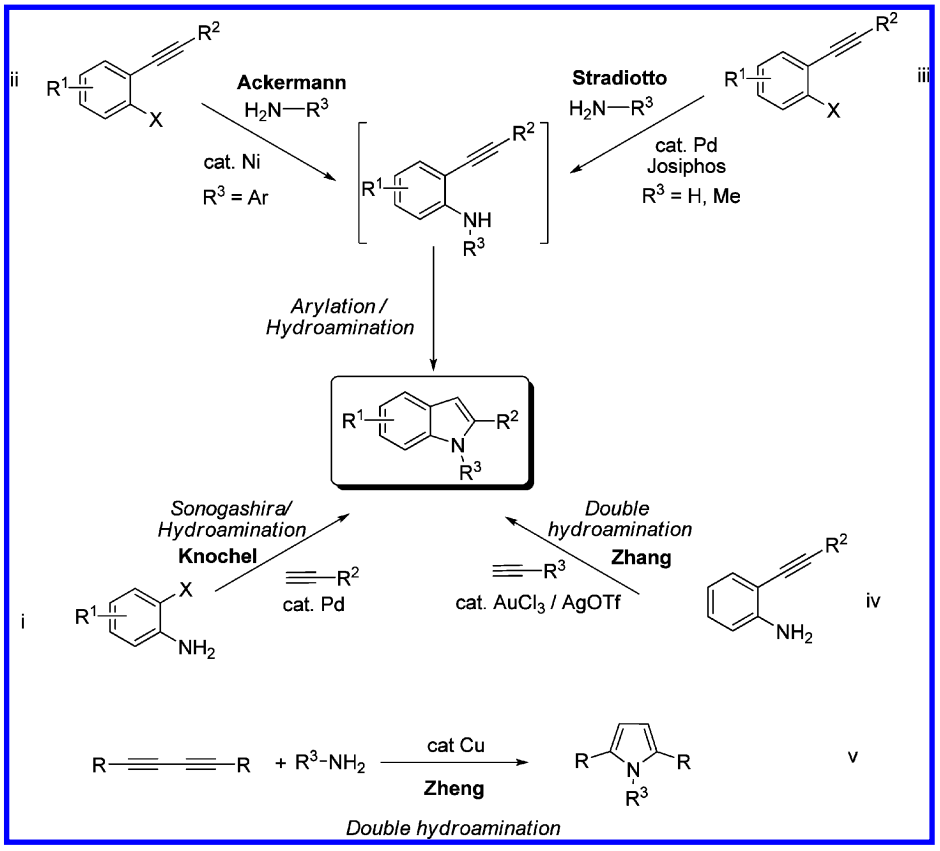


Figure 1. Significant examples of isoquinoline and naphthyridine containing natural products and pharmaceuticals.

Scheme 1. Synthesis of Indoles/Pyrroles by Inter- or Intramolecular Hydroamination of Alkynes



Nitrogen containing tetracyclic and tricyclic structures and their reduced and oxidized forms occur widely among natural products (Figure 1, i–iii),[8] biologically active pharmaceuticals,[9] and π-conjugated functional materials, such as organic semiconductors and luminescent materials (Figure 1, vi).[10] Similarly, naphthyridines are known to be an important class of heterocycles, present in many natural[11] and designed synthetic products of therapeutic importance (Figure 1, iv, v). They are associated with a wide spectrum of biological activities like anticancer,[12] antiherpes,[13] anti-HIV-1,[14] antimicrobial,[15] and adrenoceptor blocking activities.[16] Naphthyridines and their derivatives are also used as luminescence materials in molecular recognition because of their rigid planar structure.[17] The reported methods for the synthesis of indolo-, pyrrolo[2,1-*a*]isoquinolines and naphthyridines typically require multistep syntheses and expensive reagents;[18,19] a need for simple and versatile methodologies for their efficient synthesis from simple, inexpensive and readily available starting materials attracts the interest of synthetic chemists.

In the past two decades, hydroamination of alkenes, alkynes, and related unsaturated substrates is growing as a powerful technique for the synthesis of small heterocyclic molecules, natural products, enamines and imines.[20] Addition of amines on alkynes has been reported by both catalytic and noncatalytic methods to overcome the high activation energy required for this process.[21] Variety of natural products are known to involve the hydroamination of alkynes for their synthesis.[22] A considerable progress has been made by Knochel,[23a,b] Ackermann,[5c–g,23c–g] Stradiotto[23h] and others[23i–m] for the tandem synthesis of diversely substituted indoles from *ortho*-haloanilines by the

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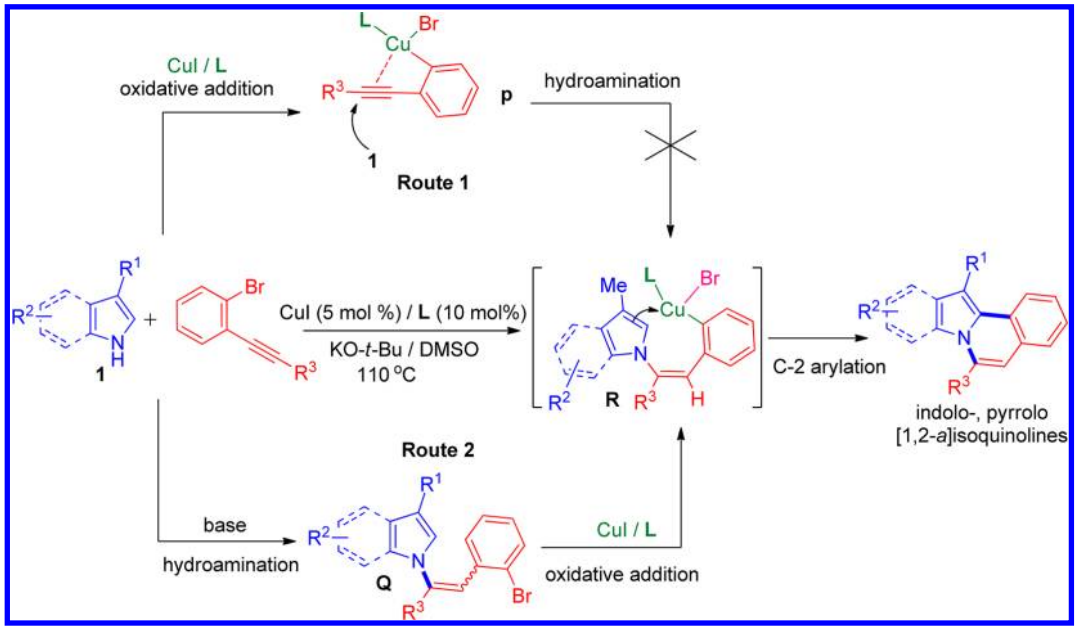
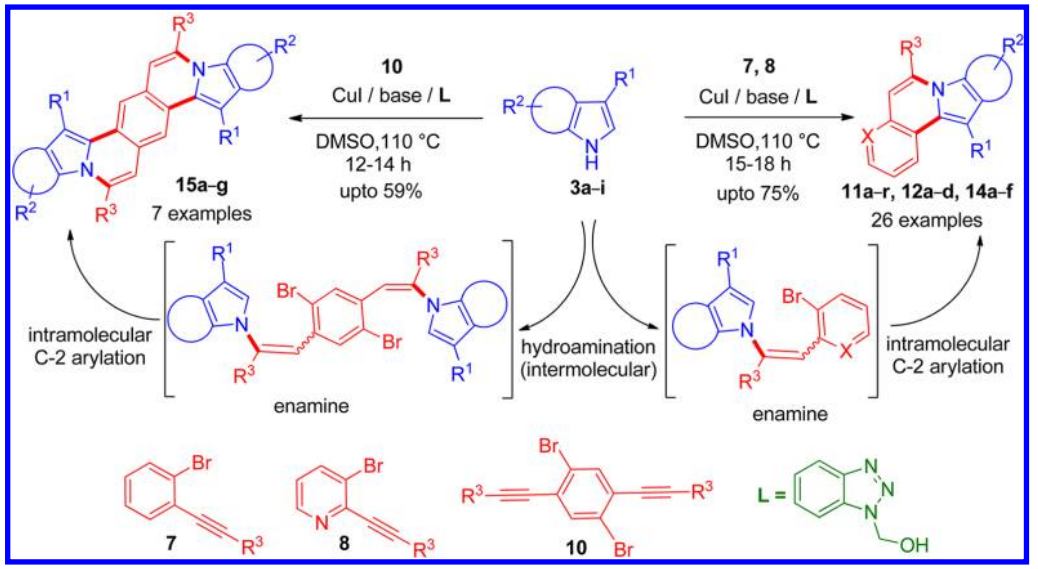
Scheme 2. Tandem Synthesis of Indolo-, Pyrrolo[2,1-*a*]isoquinolines via Intermediate R



Scheme 3. Synthesis of Fused Isoquinolines, Naphthyridines and Bisindoloisoquinolines via Preferential Hydroamination and Intramolecular C-2 Arylation



inter- or intramolecular hydroamination of alkynes (Scheme 1). Knochel and co-workers reported an elegant access to indoles from 2-haloanilines by the Sonogashira coupling followed by the base-catalyzed (KO*t*Bu, KH and CsO*t*Bu) intramolecular hydroamination.[23a,b] Ackerman[23a−g] and Stradiotto[23h] reported the tandem synthesis of indoles from the *ortho*-haloarylalkynes and anilines via arylation followed by the intramolecular hydroamination using Ni or Pd catalyst under mild reaction condition (Scheme 1, ii and iii). A highly efficient double hydroamination reaction of *o*-alkynylanilines with terminal alkynes leading to *N*-alkenylindoles was developed by Zhang et al. using gold(III) catalyst (Scheme 1, iv).[24a] Recently, Zheng et al. reported an inter- and intramolecular double hydroamination of primary amines with 1,3-butadiynes in the presence of CuCl at 100 °C to afford 1,2,5-trisubsituted pyrroles (Scheme 1, v).[24b]

In continuation of our ongoing work in the development of benzotriazole based ligands[25] and synthesis of nitrogen heterocycles by the electrophilic cyclization of alkynes,[26] recently we reported the first copper-catalyzed tandem synthesis of indolo- and pyrrolo[2,1-*a*]isoquinolines via intermolecular addition of *N*-heterocycles onto the *ortho*-haloarylalkynes followed by the intramolecular C-2 arylation.[27] The results of our recent study, base-mediated regioselective hydroamination and preferential addition of *N*-heterocycles onto the *halo*-substituted arylalkynes suggests that the mechanism of the copper-catalyzed tandem synthesis of indolo- and pyrrolo[2,1-*a*]isoquinolines proceeds via generation of intermediate **Q** through hydroamination followed by the oxidative addition to the key intermediate **R** and not vice versa (Scheme 2, route 2).[28] Herein, we wish to report the full details of our study on the copper-catalyzed tandem synthesis of indolo[2,1-*a*]isoquinolines **11a−r**, pyrrolo[2,1-*a*]isoquinolines **12a−d**, indolo/pyrrolo[2,1-*f*][1,6]naphthyridines **14a−f** and bisindolo, pyrrolo[2,1-*a*]isoquinolines **15a−g** via preferential addition of heterocyclic amines **3a−i** onto the *ortho*-

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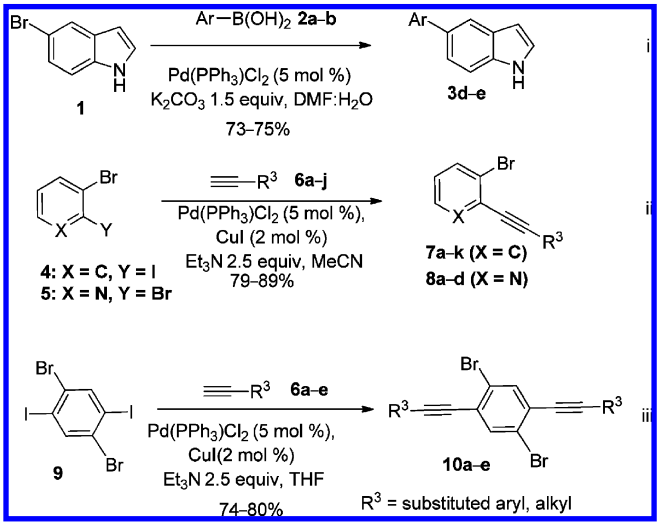
haloarylalkynes over *N*-arylation followed by the intramolecular cyclization of the in situ generated enamine by C-2 arylation using inexpensive hydroxymethyl benzotriazole as ligand (Scheme 3).

RESULTS AND DISCUSSION

Preparation of 5-Substituted Indoles and *ortho*-Haloarylalkynes. Indoles **3d,e** required for the reaction were prepared in good yield by the Suzuki-coupling of 5-bromoindole **1** with arylboronic acid **2a,b** using the standard procedure (Scheme 4).[29] The *o*-haloarylalkynes **7a−k**, **8a−d** and **10a−e**

Scheme 4. Preparation of *ortho*-Haloarylalkynes and 5-Substituted Indoles



required for examining the scope and generality of this chemistry were readily prepared by the standard Sonogashira-coupling of the commercially available 2-bromoiodobenzene (**4**), 2,3-dibromopyridine (**5**) and 1,4-dibromo-2,5-diiodobenzene (**9**) with terminal alkynes (Scheme 4).[30]

Synthesis of Indolo- and Pyrrolo[2,1-*a*]isoquinolines. Our preliminary study revealed that the optimal reaction condition for the synthesis of diversely substituted indolo[2,1-*a*]isoquinolines was 5 mol % of CuI, 10 mol % **L**, 1.4 equiv of KO*t*Bu in DMSO at 110 °C. Using the above reaction conditions, scope and limitations of this copper-catalyzed tandem process was next explored by employing various substituted *ortho*-haloarylalkynes **7a−k** and *N*-heterocycles **3a−i** (Table 1, entries 1−22). The nature of the *N*-heterocycles (electron rich, neutral and electron deficient) and the substituents attached to the triple bond has a major impact on the success of the developed chemistry. The presence of electron-releasing group (R^3) on the arenes *para* to the triple bond increases the electron density on the distal end of the triple bond and favors the formation of 6-*endodig* cyclized products.

Alkyne **7a,b** and **7e,f** bearing and electron-releasing group on the arenes *para* to the triple bond afforded the desired products **11a,b**, **11d**, **11f−k**, **11m**, and **12c** in good yields (Table 1, entries 1−2, 4, 6−11, 13, 21). Alkyne **7c** with ^{t}Bu group at 4-position of the aryl ring attached to triple bond was found favorable for the reaction and afforded the product **11c** and **12d** in 70 and 73% yields, respectively (entries 3 and 22). Alkyne **7h** having a methoxy group at 3-position of aryl ring afforded the desired products **11n**, comparatively in lower yields (entry 14). An alkyne bearing an electron-rich heterocycle, such as a thiophene, proved favorable for the reaction (entry 5). Alkyne **7g** and **7i** bearing a phenyl and phenoxy group at 4-position of the aryl ring afforded the product **11l** and **11o** in 65 and 58% yields, respectively (entries 12 and 15). The reason for the low yield of the product **11o** from alkyne **7i** might be due to the sharing of oxygen electrons by both the aryl rings (compare entries 15 and 13). Alkyne **7k** bearing a bulky electron-releasing naphthyl group provided the product **12a** in 69% yield (entry 19). However, the presence of an alkyl group on alkyne **7j** failed to afford the desired product **11q** (entry 17). We could isolate the unreacted alkyne **7j** in 90% yield; the reason might be the catalytic system used for the above transformation is not sufficient for the addition of N-heterocycles on the alkynes bearing an alkyl group.

It is important to note that the nature of the heterocyclic amines and electronic bias of the groups on both carbons of the triple bond play important role for the success of the designed chemistry (Figure 2). Effect of the electron-releasing group on the arenes *para* to the triple bond increases the electron density on the distal end (C_p) of the triple bond and favors the formation of 6-*endodig* cyclized products. 3-Methylindole **3a** bearing an electron-releasing methyl group in the 3-position of the indole was found to increase the efficiency of the transformation and afforded the cyclized products in good yields; however, indole **3b** afforded the products comparatively in lower yield (Table 1, compare entries 2 and 4). The presence of a methyl group at 3 position of the indole (Figure 2, **B**) increases the nucleophilicity at C-2 position of indole ring system, which facilitates the intramolecular cyclization via formation of tertiary carbocation, whereas in the case of unsubstituted indole (Figure 2, **C**), decomposition occurred, which might be due to the proton loss or polymerization.[26b,31] Presence of an electron-withdrawing cyano group in the 3-position of the indole provided an inseparable mixture of unidentifiable compounds (Table 1, entry 16). The reason might be the reduced nucleophilicity of the heterocycles due to presence of strong −I and −R effect of the cyano group (Figure 2, **D**).

Heterocycles **3c−e** bearing electron-releasing methoxy, 4-ethylphenyl and 4-methoxyphenyl group in 5-position of the indole were also found suitable for the reaction (Table 1, entries 6−15). However, an inseparable mixture of unidentifiable compounds was obtained when the reaction was carried out with tryptamine **3g** (Table 1, entry 18). Electron-rich heterocycles pyrrole **3h** was found suitable for the reaction and afforded the desired products **12a−d** in good yield (Table 1, entries 19−22); however, electron-deficient imidazole **3i** failed to afford the desired product **13** (Table 1, entry 23).

The products of the reaction were fully characterized by ^{1}H and ^{13}C NMR and mass spectroscopic data. The disappearance of one proton in ^{1}H NMR of *N*-heterocycles at C-2 position and two characteristic peaks of an alkyne in the ^{13}C NMR spectrum confirmed the formation of cyclized compound. The structure of the products was further confirmed by the X-ray analysis of compounds **12b** (see Supporting Information Figure S1).

Synthesis of Naphthyridines. Naphthyridines exhibit interesting biological activities and have always been an area of interest for the synthetic chemists and biologists;[11−17] to ascertain the generality and scope of the developed chemistry, we designed the direct synthesis of indolo/pyrrolo[2,1-*f*][1,6]-naphthyridines from simple and readily available starting material. To identify the optimal reaction conditions for the synthesis of naphthyridines, we examined the reaction of 3-methylindole (**3a**) with 3-bromo-2-(*p*-tolylethynyl)pyridine (**8a**) using our previously optimized condition 5 mol % of CuI,

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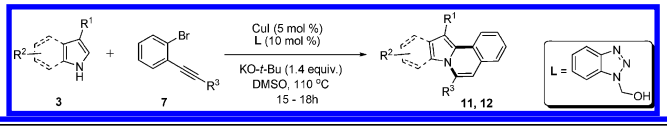
Table 1. Tandem Synthesis of Indolo- and Pyrrolo[2,1-*a*]isoquinolines[a]



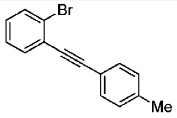
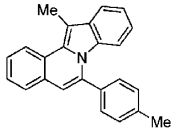
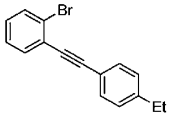
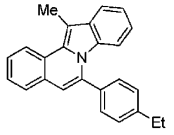
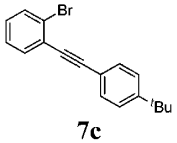
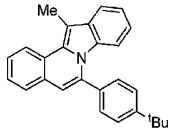
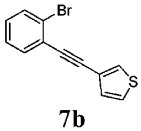
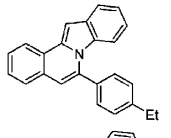
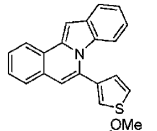
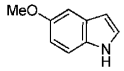
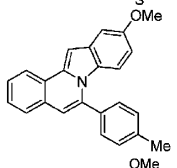
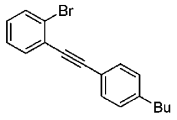
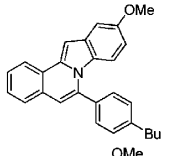
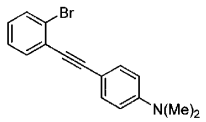
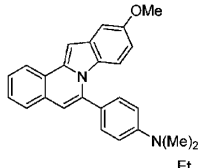
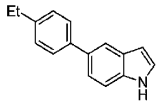
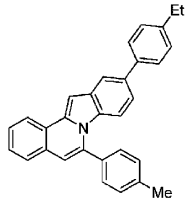
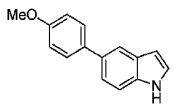
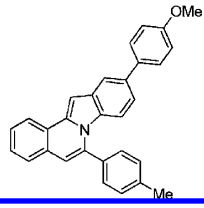
entry	*N*-heterocycle	alkyne	product		yield(%)[b]
1	 **3a**	 **7a**		**11a**	75
2	**3a**	 **7b**		**11b**	74
3	**3a**	 **7c**		**11c**	70
4	 **3b**	 **7b**		**11d**	65
5	**3b**	**7d**		**11e**	63
6	 **3c**	**7a**		**11f**	66
7	**3c**	 **7e**		**11g**	65
8	**3c**	 **7f**		**11h**	62
9	 **3d**	**7a**		**11i**	67
10	 **3e**	**7a**		**11j**	63

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Table 1. continued

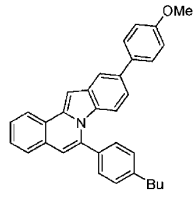
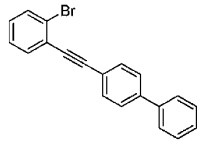
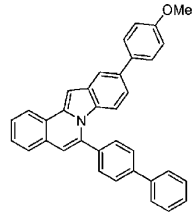
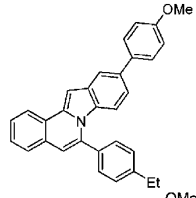
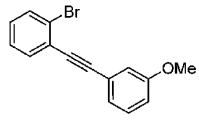
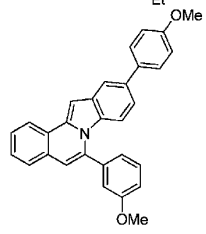
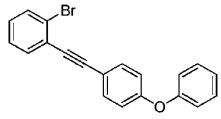
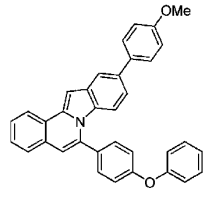
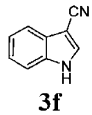
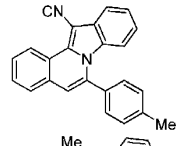
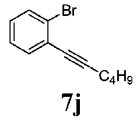
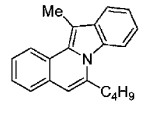
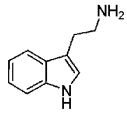
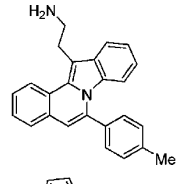
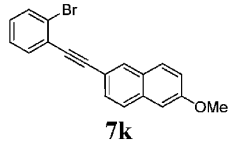
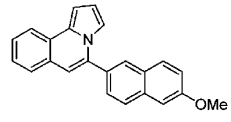
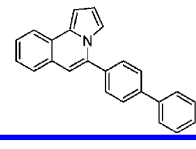
entry	*N*-heterocycle	alkyne	product		yield(%)[b]
11	3e	7e		11k	73
12	3e	 7g		11l	65
13	3e	7b		11m	70
14	3e	 7h		11n	69
15	3e	 7i		11o	58
16	 3f	7a		11p	[d] –
17	3a	 7j		11q	nr[c]
18	 3g	7a		11r	[d] –
19	 3h	 7k		12a	69
20	3h	7g		12b	71

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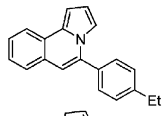
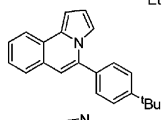
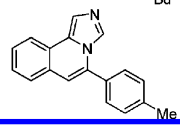
Table 1. continued

entry	*N*-heterocycle	alkyne	product		yield(%)[b]
21	3h	7b		12c	75
22	3h	7c		12d	73
23	 3i	7a		13	d —

[a]All the reactions were carried out using 0.5 mmol of the *N*-heterocycle **3** and 1.1 equiv of 2-haloarylalkyne **7** in the presence of CuI (5.0 mol %), **L** (10 mol %), and the base (1.4 equiv), in 2 mL of DMSO at 110 °C. [b]Yield. [c]No reaction. [d]An inseparable mixture was obtained.

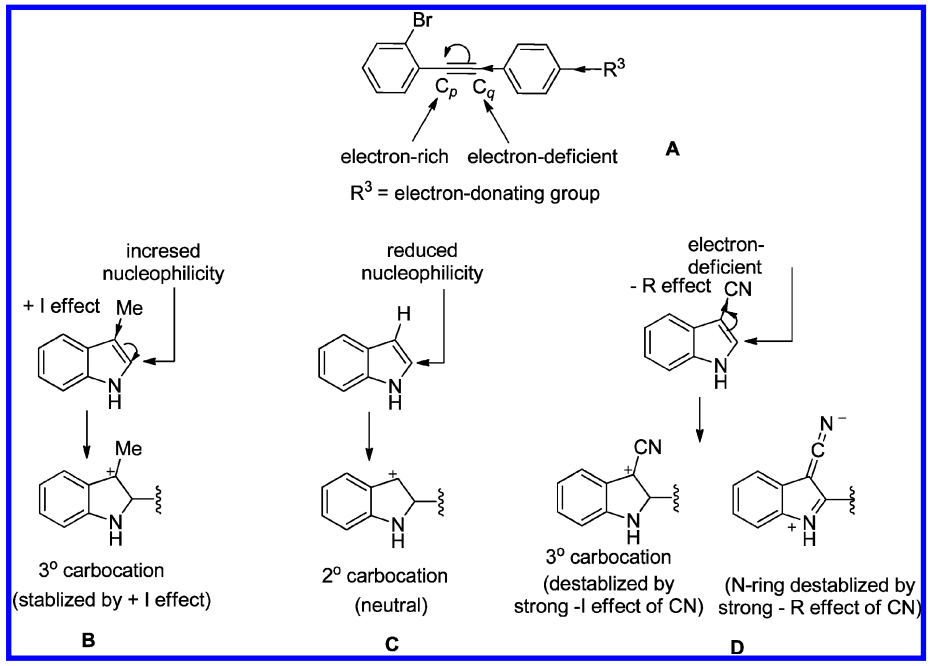


Figure 2. Effect of substituents and *N*-heterocycles on the reaction.

10 mol % **L**, 1.4 equiv of KO*t*-Bu in DMSO at 110 °C. Using the above reaction conditions, product **14a** was obtained in 24 and 37% yields, respectively, after running the reaction for 8 and 12 h (Table 2, entries 1−2). The yield of the product remained almost same after 18 and 24 h (entries 3−4). However, increasing the catalyst loading from 5 to 10 mol % and ligand from 10 to 20 mol % afforded the desired product **14a** in 74% yield (entry 5). Decreasing the reaction time from 18 to 12 h afforded the desired compound in lower yield (entries 6 and 7). From entries 8 to 11, it is apparent that DMSO was found to be quite successful for the transformation. Other bases like K_3PO_4 and NaO*t*-Bu afforded the product **14a** in 67 and 70% yields, respectively (entries 12−13). When we carried out reaction in the absence of ligand, the desired product was not observed (entry 14).

After optimizing the reaction condition, we examined the scope and generality of the reaction by utilizing a variety of alkynes **8a−d** (Table 3, entries 1−6). Electron-rich heterocycles 3-methylindole **3a** and pyrrole **3g** afforded the desired naphthyridines **14a**,**b**, and **14f** in good yield in comparison to indole (entries 1−2, 6 vs 3−4). 5-Methoxyindole **3c** afforded the cyclized products **14d−e** with alkyne **8c** and **8d** in 69 and 70% yields, respectively (Table 3, entries 4 and 5).

Synthetic Application: Synthesis of Bisindolo- and Pyrrolo[2,1-*a*]isoquinolines. Success of the designed chemistry in the synthesis of indolo, pyrrolo[2,1-*a*]isoquinolines and naphthyridines encouraged us for the direct synthesis of bisindolo[2,1-*a*]isoquinolines, a regioisomer of bisindolo[2,1-*a*]quinolines used as single-crystal field-effect transistor.[32] Under the optimized reaction conditions (Table 2, entry 6), reaction of heterocycles **3a**,**b**, **3g** with 2,5-dibromo-dialkyne **10a−e**, afforded the desired bisindolo-, pyrrolo[2,1-*a*]isoquinolines **15a−g** in moderate yields (Table 4, entries 1−7). The reason for the low yield of the products might be due to the possible formation of more no of hydroaminated products as well as monocyclized product. We observed that reaction of **3a** with dialkyne **10a**, afforded the biscyclized product **15a** in 49% yield along with the monocyclized product **16a** in 29% yield (entry 1). Electron-rich small heterocycles, pyrrole **3g** afforded the biscyclized products comparatively in better yield with respect to indole and 3-methylindole.

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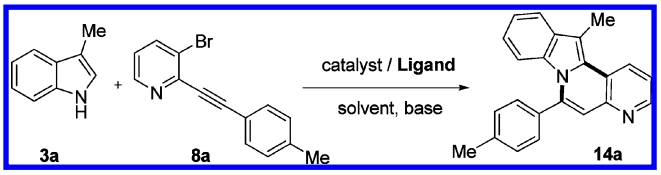
Table 2. Optimization of Reaction Conditions for the Tandem Synthesis of Naphthyridines[a]



entry	catalyst (mol %)	L (mol %)	base	solvent	*t* (h)	yield (%)
1	CuI/5	L/10	KO*t*-Bu	DMSO	8	24
2	CuI/5	L/10	KO*t*-Bu	DMSO	12	37
3	CuI/5	L/10	KO*t*-Bu	DMSO	18	39
4	CuI/5	L/10	KO*t*-Bu	DMSO	24	40
5	CuI/10	L/20	KO*t*-Bu	DMSO	24	74
6	**CuI/10**	**L/20**	**KO*t*-Bu**	**DMSO**	**18**	**74**
7	CuI/10	L/20	KO*t*-Bu	DMSO	12	64
8	CuI/10	L/20	KO*t*-Bu	DMF	18	65
9	CuI/10	L/20	KO*t*-Bu	DMA	18	53
10	CuI/10	L/20	KO*t*-Bu	Dioxane	18	48
11	CuI/10	L/20	KO*t*-Bu	Toluene	18	45
12	CuI/10	L/20	K_3PO_4	DMSO	18	67
13	CuI/10	L/20	NaO*t*-Bu	DMSO	18	70
14	CuI/10		KO*t*-Bu	DMSO	18	00

[a]The reactions were performed using **3a** (0.5 mmol) with 3-bromo-2-(*p*-tolylethynyl)pyridine **8a** (1.1 equiv) in 2.0 mL of solvent at 110 °C under an nitrogen atmosphere.

Conclusion. In conclusion, we have described a direct approach for the copper-catalyzed tandem synthesis of medicinally important indolo-, pyrrolo[2,1-*a*]isoquinolines and naphthyridines in good yields with high regioselectivity by the preferential addition of heterocyclic amines onto the *ortho*-haloarylalkynes over *N*-arylation followed by intramolecular cyclization of the in situ generated enamine by C-2 arylation. Application of developed chemistry has been successfully extended for the direct synthesis of heptacyclic bisindolo-, pyrrolo[2,1-*a*]isoquinolines, which is a regioisomer of bisindolo-[2,1-*a*]quinolines used as single-crystal field-effect transistor. An inexpensive and air stable compound hydroxymethyl benzotriazole ($BtCH_2OH$) has been used as a ligand, along with Cu(I), increasing the overall utility of this reaction. From a synthetic point of view, the net transformation involves a one-step conversion of simple, inexpensive and readily available starting materials into interesting class of heterocyclic compounds, natural-product-like compounds and organic materials. This chemistry is expected to find application in organic synthesis in general, and in the construction of a variety of interesting fused π-conjugated compounds.

EXPERIMENTAL SECTION

General Method. ^{1}H NMR (300 MHz, 400 MHz) and ^{13}C NMR (75 MHz, 100 MHz) spectra were recorded in $CDCl_3$ and DMSO-d_6. 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 on 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. All melting points are uncorrected.

General Procedure for the Palladium-Catalyzed Synthesis of Substituted Indoles 3d–e. The 5-substituted indoles were prepared by the Suzuki coupling of the corresponding arylboronic acids with 5-bromoindole using reported procedures.[29] The structure and purity of the known starting materials **3e** was confirmed by the comparison of their physical and spectral data (^{1}H NMR, ^{13}C NMR, and HRMS) with those reported in the literature.[29]

*5-(p-Ethylphenyl)-1H-indole (**3d**).* The product was obtained as white needles (80.70 mg, 73% yield): mp 66–68 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.10 (brs, 1H), 7.84 (s, 1H), 7.57 (dd, J = 8.4 and 5.4 Hz, 2H), 7.46–7.42 (m, 2H), 7.27 (d, J = 8.4 Hz, 2H), 7.25–7.20 (m, 1H), 6.60 (t, J = 2.4 Hz, 1H), 2.69 (q, J = 7.8 Hz, 2H), 1.28 (t, J = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.3, 139.9, 135.1, 133.4, 128.3, 128.2, 127.3, 124.8, 121.9, 119.0, 111.2, 102.9, 28.5, 15.6; HRMS Calcd for $C_{16}H_{15}N$ (M + H$^+$) 221.1204, found 221.1204.

General Procedure for the Synthesis of 2-Haloarylalkynes 7a–k, 8a–d, 10a–e. The *o*-haloarylalkynes **7a–k**, **8a–d** and **10a– e** were readily prepared by the coupling reaction of corresponding aryl-halides with terminal alkynes using reported procedures.[30] The structure and purity of known starting materials **7a**,[30a] **7c**,[30b] **7d**,[30c] **7f**,[30c] **7g**[30d] and **7j**[30e] were confirmed by comparison of their physical and spectral data (^{1}H NMR, ^{13}C NMR, and HRMS) with those reported in the literature.

*1-Bromo-2-((p-ethylphenyl)ethynyl)benzene (**7b**).* The product was obtained as a colorless liquid (124.00 mg, 88% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.61 (d, J = 8.7 Hz, 1H), 7.56–7.49 (m, 3H), 7.31–7.29 (m, 1H), 7.21–7.14 (m, 3H), 2.69 (dd, J = 6.0 and 9.0 Hz, 2H), 1.25(t, J = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.2, 133.1, 132.5, 132.4, 131.7, 129.2, 128.0, 127.9, 127.0, 125.6, 120.1, 94.2, 87.4, 28.9, 15.4; HRMS Calcd for $C_{16}H_{13}Br$ (M + H$^+$) 284.0201, found 284.0202.

*1-Bromo-2-((p-butylphenyl)ethynyl)benzene (**7e**).* The product was obtained as a yellow oil (132.6 mg, 85% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.87 (d, J = 7.6 Hz, 1H), 7.53–7.43 (m, 3H), 7.40–7.29 (m, 1H), 7.17 (d, J = 7.8 Hz, 2H), 6.99 (m, 1H), 2.69 (t, J = 7.5 Hz, 2H), 1.64 (q, J = 7.5 Hz, 2H), 1.40 (t, J = 7.5 Hz, 2H), 0.85 (t, J = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.9, 138.7, 132.4, 132.3, 131.5, 129.9, 129.2, 127.8, 119.8, 101.2, 93.3, 91.1, 35.6, 33.5, 29.7, 22.3, 14.0; HRMS Calcd for $C_{18}H_{17}Br$ (M + H$^+$) 312.0514, found 312.0514.

*1-Bromo-2-((m-methoxyphenyl)ethynyl)benzene (**7h**).* The product was obtained as a yellow oil (113.0 mg, 79% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.62 (d, J = 7.8 Hz, 1H), 7.55 (d, J = 7.5 Hz, 1H), 7.31–7.24 (m, 2H), 7.18 (d, J = 7.8 Hz, 2H), 7.00 (s, 1H), 6.93–6.89 (m, 1H), 3.83 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.4, 133.2, 132.4, 129.8, 129.4, 127.0, 125.7, 125.3, 124.3, 123.9, 116.4, 115.3, 93.8, 87.8, 55.3; HRMS Calcd for $C_{15}H_{11}BrO$ (M + H$^+$) 285.9993, found 285.9994.

*1-Bromo-2-((p-phenoxyphenyl)ethynyl)benzene (**7i**).* The product was obtained as white needles (140.95 mg, 81% yield): mp 64–65 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.61 (d, J = 7.8 Hz, 1H), 7.54 (d, J = 8.7 Hz, 3H), 7.40–7.34 (m, 2H), 7.31–7.28 (m, 1H), 7.19–7.13 (m, 2H), 7.05 (d, J = 7.8 Hz, 2H), 6.98 (d, J = 8.7 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.9, 156.3, 133.4, 133.1, 132.5, 129.9, 129.3, 127.1, 125.6, 125.5, 123.9, 119.5, 118.4, 117.4, 93.6, 87.5; HRMS Calcd for $C_{20}H_{13}BrO$ (M + H$^+$) 348.0150, found 348.0151.

*2-((o-Bromophenyl)ethynyl)-6-methoxynaphthalene (**7k**).* The product was obtained as white needles (132.72 mg, 79% yield): mp 83–84 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.03 (s, 1H), 7.71 (dd, J = 3.0 and 5.1 Hz, 2H), 7.61 (dd, J = 8.0 and 2.4 Hz, 3H), 7.32–7.27 (m, 1H), 7.20–7.12 (m, 3H), 3.92 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.5, 134.4, 133.2 132.4, 131.5, 129.4, 129.2, 128.9, 128.5, 127.1, 126.9, 125.6, 119.5, 117.8, 105.8, 94.6, 87.7, 55.4; HRMS Calcd for $C_{19}H_{13}BrO$ (M + H$^+$) 336.0150, found 336.0151.

*3-Bromo-2-(p-tolylethynyl)pyridine (**8a**).* The product was obtained as a yellow oil (111.1 mg, 82% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.55–8.52 (m, 1H), 7.93–7.90 (m, 1H), 7.56 (d, J = 8.1 Hz, 2H), 7.35 (s, 1H), 7.23 (d, J = 8.1 Hz, 1H), 7.10 (dd, J = 4.5 and 3.6 Hz, 1H), 2.38 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.9, 138.7, 132.4, 132.3, 131.5, 130.0, 129.2, 127.8, 119.8, 101.2, 93.3, 91.1, 21.6; HRMS Calcd for $C_{14}H_{10}BrN$ (M + H$^+$) 270.9997, found 270.9998.

*3-Bromo-2-((4-ethylphenyl)ethynyl)pyridine (**8b**).* The product was obtained as a yellow oil (121.1 mg, 85% yield): ^{1}H NMR (300 MHz,

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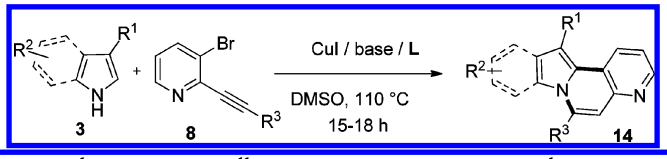
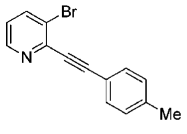
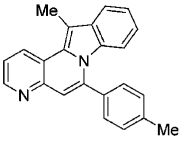
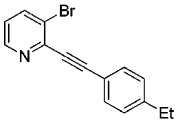
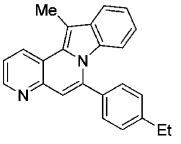
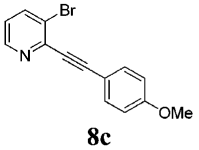
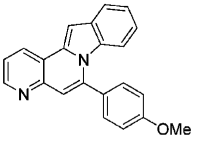
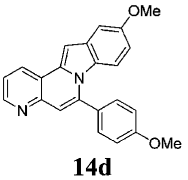
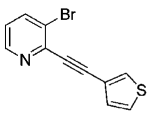
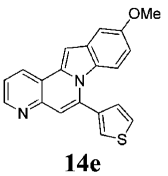
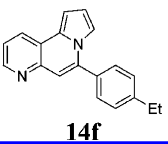
Table 3. Synthesis of Indolo- and Pyrrolo[2,1-*f*][1,6]naphthyridines[a]



entry	*N*-heterocycle	alkyne	product	yield (%)
1	**3a**	 **8a**	 **14a**	74
2	**3a**	 **8b**	 **14b**	72
3	**3b**	 **8c**	 **14c**	65
4	**3c**	**8c**	 **14d**	69
5	**3c**	 **8d**	 **14e**	70
6	**3g**	**8b**	 **14f**	73

[a]The reactions were performed using *N*-heterocycle **3** (0.5 mmol), 1.1 equiv of 2-haloarylalkyne **8**, CuI (10 mol %), **L** (20 mol %), and 1.4 equiv of KO*t*-Bu in 2.0 mL of DMSO at 110 °C for 18 h.

$CDCl_3$) δ 8.55−8.53 (m, 1H), 7.93−7.89 (m, 1H), 7.57 (d, J = 8.1 Hz, 2H), 7.36 (s, 1H), 7.22 (d, J = 8.1 Hz, 1H), 7.11(dd, J = 4.5 and 3.6 Hz, 1H), 2.68 (q, J = 7.5 Hz, 2H), 1.25 (t, J = 7.5 Hz, 3H); ^{13}C NMR(75 MHz, $CDCl_3$) δ 148.2, 145.8, 139.7, 132.1, 128.3, 127.9, 123.7, 123.3, 119.1, 94.5, 86.9, 28.9, 15.2; HRMS Calcd for $C_{15}H_{12}BrN$ (M + H^+) 285.0153, found 285.0154.

*3-Bromo-2-((4-methoxyphenyl)ethynyl)pyridine (**8c**).* The product was obtained as brown needles (116.2 mg, 81% yield): mp 63−64 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (dd, J = 1.4 and 3.2 Hz, 1H), 7.92 (dd, J = 1.2 and 6.8 Hz, 1H), 7.60 (d, J = 8.8 Hz, 2H), 7.10 (q, J = 4.3 Hz, 1H), 6.91 (d, J = 8.8 Hz, 2H), 3.84 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.7, 148.4, 144.1, 139.9, 134.0, 123.7, 123.4, 114.3, 114.1, 94.7, 86.7, 55.6; HRMS Calcd for $C_{14}H_{10}BrNO$ (M + H^+) 286.9946, found 286.9945.

*3-Bromo-2-(thiophen-3-ylethynyl)pyridine (**8d**).* The product was obtained as a yellow oil (111.7 mg, 85% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (dd, J = 1.4 and 4.6 Hz, 1H), 7.79 (dd, J = 1.4 and 8.2 Hz, 1H), 7.60−7.59 (m, 1H), 7.23−7.21 (m, 1H), 7.19−7.17 (m, 1H), 7.01−6.98 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.6, 143.0, 139.2, 130.2, 129.3, 125.1, 122.9, 122.8, 120.4, 88.7, 86.5; HRMS Calcd for $C_{11}H_6BrNS$ (M + H^+) 262.9404, found 262.9404.

*4,4′-(2,5-Dibromo-1,4-phenylene)bis(ethyne-2,1-diyl)bis-(ethylbenzene) (**10a**).* The product was obtained as white needles (191.1 mg, 78% yield): mp 176−178 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75 (s, 2H), 7.49 (d, J = 8.1 Hz, 4H), 7.20 (d, J = 8.1 Hz, 4H), 2.67 (q, J = 7.5 Hz, 4H), 1.24 (t, J = 7.5 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.7, 136.5, 135.9, 135.2, 132.3, 131.7, 129.7, 128.0, 127.3, 125.5, 125.3, 123.8, 122.5, 120.0, 119.6, 119.3, 119.0, 114.2, 111.7, 95.7, 86.5, 28.9,

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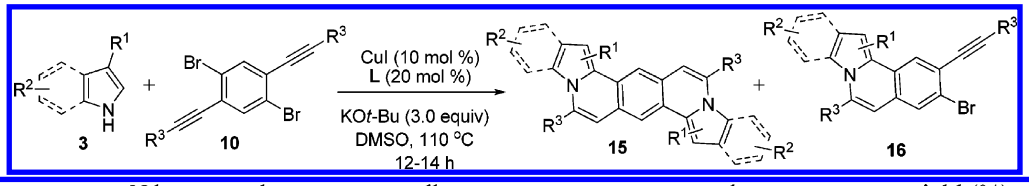
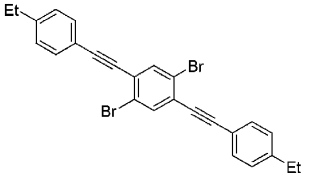
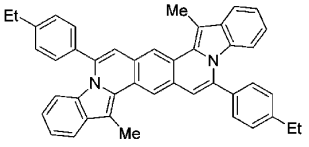
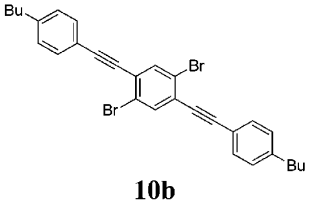
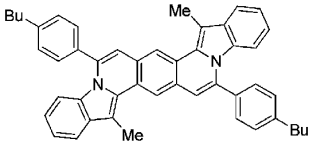
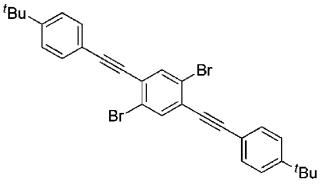
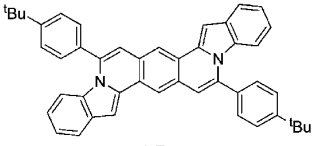
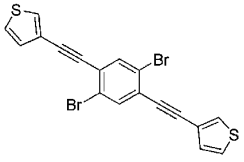
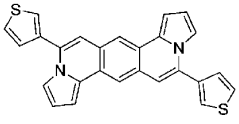
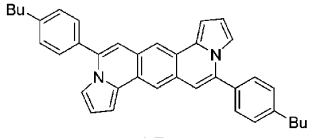
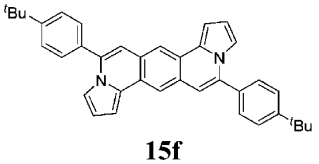
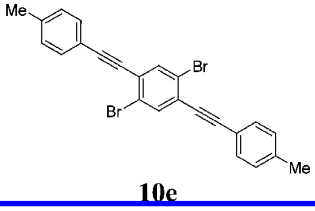
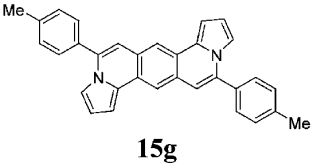
Table 4. Synthesis of Bisindolo- and Pyrrolo[2,1-*a*]isoquinolines[a]



entry	*N*-heterocycle	alkyne	product	yield (%)
1	**3a**	 **10a**	 **15a**	49
2	**3a**	 **10b**	 **15b**	46
3	**3b**	 **10c**	 **15c**	45
4	**3g**	 **10d**	 **15d**	57
5	**3g**	**10b**	 **15e**	59
6	**3g**	**10c**	 **15f**	58
7	**3g**	 **10e**	 **15g**	54

[a]The reactions were performed using *N*-heterocycle **3** (0.5 mmol), *bis*-dihaloarylalkyne **10** (0.5 equiv), CuI (10 mol %), **L** (20 mol %), and KO*t*-Bu (3.0 equiv) in 2.0 mL of DMSO at 110 °C for 12−14 h.

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28.7, 15.4, 15.3; HRMS Calcd for $C_{26}H_{20}Br_2$(M + H$^+$) 489.9932, found 489.9934.

*4,4′-(2,5-Dibromo-1,4-phenylene)bis(ethyne-2,1-diyl)bis-(butylbenzene) (**10b**).* The product was obtained as white needles (207.5 mg, 76% yield): mp 118−120 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (s, 2H), 7.46 (d, J = 8.1 Hz, 4H), 7.16 (d, J = 8.1 Hz, 4H), 2.61 (t, J = 8.1 Hz, 4H), 1.63−1.57 (m, 4H), 1.37−1.31 (m, 4H), 0.92 (t, J = 7.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.4, 135.8, 135.1, 131.7, 128.6, 126.4, 123.6, 119.4, 108.9, 96.9, 86.3, 35.7, 33.3, 22.3, 13.9; HRMS Calcd for $C_{30}H_{28}Br_2$ (M + H$^+$) 546.0558, found 546.0558.

*4,4′-(2,5-Dibromo-1,4-phenylene)bis(ethyne-2,1-diyl)bis(tert-butylbenzene) (**10c**).* The product was obtained as white needles (202.0 mg, 74% yield): mp 202−204 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (s, 2H), 7.50 (d, J = 8.1 Hz, 4H), 7.38 (d, J = 8.1 Hz, 4H), 1.32 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.5, 135.8, 131.5, 126.4, 125.5, 123.6, 119.3, 96.8, 86.3, 34.8, 31.1; HRMS Calcd for $C_{30}H_{28}Br_2$ (M + H$^+$) 546.0558, found 546.0558.

*3,3′-(2,5-Dibromo-1,4-phenylene)bis(ethyne-2,1-diyl)dithiophene (**10d**).* The product was obtained as white needles (178.3 mg, 80% yield): mp 151−152 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (s, 2H), 7.58 (d, J = 3.0 Hz, 2H), 7.32−7.30 (m, 2H), 7.20 (d, J = 5.2 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 135.9, 129.9, 129.7, 126.3, 125.7, 123.5, 121.4, 91.8, 86.3; HRMS Calcd for $C_{18}H_8Br_2S_2$ (M + H$^+$) 445.8434, found 445.8435.

*4,4′-(2,5-Dibromo-1,4-phenylene)bis(ethyne-2,1-diyl)bis-(methylbenzene) (**10e**).* The product was obtained as white needles (173.23 mg, 75% yield): mp 190−191 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (s, 2H), 7.46 (d, J = 8.1 Hz, 4H), 7.20 (d, J = 8.1 Hz, 4H), 2.4 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.4, 135.8, 131.7, 129.2, 126.4, 123.6, 119.3, 96.9, 86.3, 21.6; HRMS Calcd for $C_{24}H_{16}Br_2$ (M + H$^+$) 461.9619, found 461.9619.

General Procedure for the Synthesis of Isoquinoline 11a−o, 12a−d. An oven-dried Schlenk tube with a Teflon screw valve was charged with CuI (5.0 mol %), **L** (10 mol %), 0.5 mmol of the *N*-heterocycle **3**, 1.1 equiv of 2-haloarylalkyne **7** and 1.4 equiv KO*t*-Bu. The Schlenk tube was capped with a rubber septum and then evacuated and backfilled with nitrogen, followed by DMSO (2.0 mL) added by syringe, through the septum. The septum was then replaced with a Teflon screw valve, and the Schlenk tube was sealed. The reaction mixture was heated to 110 °C until 2-haloarylalkyne **7** had been completely consumed (as determined by TLC) and was allowed to cool to room temperature. The reaction mixture was diluted with ethyl acetate (10 mL) and water (15 mL). Organic layer was concentrated under reduced pressure. The crude material so obtained was purified by flash chromatography on silica gel.

*12-Methyl-6-(p-tolyl)indolo[2,1-a]isoquinoline (**11a**).* The product was obtained as yellow needles (120.4 mg, 75% yield): mp 88−89 °C; ^{1}H NMR (400 MHz, DMSO) δ 8.40 (d, J = 8.0 Hz, 1H), 7.83 (d, J = 8.0 Hz, 1H), 7.66 (d, J = 8.0 Hz, 1H), 7.56−7.54 (m, 1H), 7.49−7.44 (m, 1H), 7.42−7.41 (m, 4H), 7.20 (t, J = 8.0 Hz, 1H), 6.88 (t, J = 8.3 Hz, 1H), 6.56 (s, 1H), 6.32 (d, J = 9.4 Hz, 1H), 2.82 (s, 3H), 2.46 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 139.0, 138.0, 133.3, 130.6, 130.2, 129.7, 129.6, 129.5, 129.5, 128.9, 127.1, 127.0, 126.4, 126.3, 124.1, 121.1, 120.4, 118.3, 113.7, 110.5, 104.9, 21.1, 11.5; HRMS Calcd for $C_{24}H_{19}N$ (M + H$^+$) 321.1517, found 321.1518.

*12-Methyl-6-(p-ethylphenyl)indolo[2,1-a]isoquinoline (**11b**).* The product was obtained as yellow needles (124.0 mg, 74% yield): mp 104−105 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.42 (d, J = 6.0 Hz, 1H), 7.79 (d, J = 9.0 Hz, 1H), 7.53−7.51 (m, 2H), 7.48−7.41 (m, 3H), 7.35 (d, J = 8.1 Hz, 2H), 7.27−7.18 (m, 1H), 6.91 (t, J = 6.0 Hz, 1H), 6.42 (d, J = 7.5 Hz, 2H), 2.89 (s, 3H), 2.81 (q, J = 7.5 Hz, 2H), 1.36 (t, J = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.4, 138.5, 134.2, 131.5, 130.9, 130.2, 130.1, 129.1, 128.3, 127.2, 126.6, 126.2, 124.4, 120.9, 120.3, 117.9, 114.4, 110.7, 105.4, 28.8, 15.5, 11.8; HRMS Calcd for $C_{25}H_{21}N$ (M + H$^+$) 335.1674, found 335.1674.

*12-Methyl-6-(p-tert-butylphenyl)indolo[2,1-a]isoquinoline (**11c**).* The product was obtained as yellow needles (127.1 mg, 70% yield): mp 138−140 °C; ^{1}H NMR (400 MHz, DMSO) δ 8.36 (d, J = 8.2 Hz, 1H), 7.74 (d, J = 8.2 Hz, 1H), 7.57−7.55 (m, 3H), 7.54−7.49 (m, 1H), 7.43−7.41 (m, 3H), 7.18−7.15 (m, 1H), 6.80 (t, J = 6.9 Hz, 1H), 6.48 (s, 1H), 6.29 (d, J = 6.9 Hz, 1H), 2.06 (s, 3H), 1.39 (s, 9H); ^{13}C NMR (100 MHz, DMSO+$CDCl_3$) δ 151.9, 137.7, 133.1, 130.6, 129.5, 129.3, 128.3, 126.5, 126.0, 125.4, 123.8, 120.7, 120.0, 117.7, 113.7, 110.3, 104.5, 34.4, 30.9, 11.3; HRMS Calcd for $C_{27}H_{25}N$ (M + H$^+$) 363.1987, found 363.1988.

*6-(p-Ethylphenyl)indolo[2,1-a]isoquinoline (**11d**).* The product was obtained as yellow needles (104.4 mg, 65% yield): mp 112−113 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.21 (d, J = 7.5 Hz, 1H), 7.76 (d, J = 7.8 Hz, 1H), 7.54−7.43 (m, 5H), 7.38−7.34 (m, 3H), 7.24−7.19 (m, 1H), 6.89 (t, J = 7.9 Hz, 1H), 6.49 (d, J = 9.9 Hz, 2H), 2.82 (q, J = 7.5 Hz, 2H), 1.36 (t, J = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.6, 138.5, 136.4, 133.8, 132.2, 129.5, 129.2, 129.1, 128.3, 127.5, 126.9, 126.4, 125.4, 123.3, 121.6, 120.2, 119.9, 114.6, 110.9, 94.3, 28.8, 15.5, 11.8; HRMS Calcd for $C_{24}H_{19}N$ (M + H$^+$) 321.1517, found 321.1515.

*6-(Thiophen-3-yl)indolo[2,1-a]isoquinoline(**11e**).* The product was obtained as yellow needles (94.2 mg, 63% yield): mp 130−131 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.70 (d, J = 3.9 Hz, 1H), 8.43 (d, J = 7.8 Hz, 1H), 7.79 (d, J = 7.8 Hz, 1H), 7.63−7.55 (m, 2H), 7.40−7.37 (m, 1H), 7.30−7.26 (m, 4H), 7.02 (t, J = 8.1 Hz, 1H), 6.82 (s, 1H), 6.57 (d, J = 8.7 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.6, 146.7, 137.6, 136.0, 135.1, 132.2, 130.6, 129.6, 128.5, 126.7, 125.9, 122.2, 121.7, 121.5, 121.1, 120.4, 114.2, 112.6, 96.3; HRMS Calcd for $C_{20}H_{13}NS$ (M + H$^+$) 299.0769, found 299.0769.

*10-Methoxy-6-(p-methylphenyl)indolo[2,1-a]isoquinoline (**11f**).* The product was obtained as yellow needles (116.3 mg, 69% yield): mp 133−134 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.19 (d, J = 7.5 Hz, 1H), 7.55−7.51 (m, 2H), 7.48−7.40 (m, 3H), 7.36 (d, J = 7.8 Hz, 2H), 7.27 (d, J = 5.4 Hz, 1H), 7.18 (d, J = 2.7 Hz, 1H), 6.57−6.54 (m, 1H), 6.49 (s, 1H), 6.39 (d, J = 9.3 Hz, 1H), 3.85 (s, 3H), 2.52 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.2, 139.3, 138.3, 137.0, 133.5, 130.4, 129.6, 129.2, 129.0, 127.5, 127.4, 126.9, 126.4, 125.1, 123.3, 115.4, 110.5, 110.4, 100.9, 93.9, 55.6, 21.6; HRMS Calcd for $C_{24}H_{19}NO$ (M + H$^+$) 337.1467, found 337.1466.

*10-Methoxy-6-(p-butylphenyl)indolo[2,1-a]isoquinoline (**11g**).* The product was obtained as yellow needles (123.2 mg, 65% yield): mp 89−90 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.11 (d, J = 7.5 Hz, 1H), 7.46 (d, J = 7.2 Hz, 1H), 7.41−7.31 (m, 5H), 7.27 (d, J = 7.5 Hz, 2H), 7.18 (s, 1H), 6.98 (s, 1H), 6.46−6.54 (m, 1H), 6.24 (d, J = 9.1 Hz, 1H), 3.77 (s, 3H), 2.69 (t, J = 7.5 Hz, 2H), 1.64 (q, J = 7.5 Hz, 2H), 1.40 (t, J = 7.5 Hz, 2H), 0.85 (t, J = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.2, 144.3, 138.3, 137.0, 133.7, 130.4, 129.2, 129.0, 128.9, 127.5, 127.4, 126.8, 126.3, 125.1, 123.2, 115.4, 112.1, 110.4, 100.9, 93.9, 55.6, 35.6, 33.5, 29.7, 13.9; HRMS Calcd for $C_{27}H_{25}NO$ (M + H$^+$) 379.1936, found 379.1938.

*4-(10-Methoxyindolo[2,1-a]isoquinolin-6-yl)-N,N-dimethylaniline (**11h**).* The product was obtained as yellow needles (113.5 mg, 62% yield): mp 158−159 °C; ^{1}H NMR (400 MHz, DMSO) δ 8.77−8.73 (m, 2H), 8.1 (s, 1H), 8.07−8.06 (m, 1H), 7.92−7.90 (m, 1H), 7.70 (s, 1H), 7.56−7.53 (m, 1H), 7.40−7.37 (m, 2H), 6.96 (s, 2H), 6.74 (s, 1H), 6.46 (d, J = 8.7 Hz, 1H), 3.86 (s, 6H), 3.68 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 153.2, 150.1, 145.8, 137.2, 136.7, 136.4, 135.3, 135.2, 134.5, 131.1, 129.7, 128.5, 128.0, 127.0, 122.4, 120.6, 120.4, 118.1, 113.8, 112.1, 104.3, 97.1, 60.0, 55.9; HRMS Calcd for $C_{25}H_{22}N_2O$ (M + H$^+$) 366.1732, found 366.1733.

*6-(p-Tolyl)-10-(p-ethylphenyl)indolo[2,1-a]isoquinoline (**11i**).* The product was obtained as yellow needles (137.7 mg, 67% yield): mp 158−160 °C; ^{1}H NMR (400 MHz, DMSO) δ ^{1}H NMR (300 MHz, DMSO) δ 8.36 (d, J = 7.8 Hz, 1H), 8.00 (s, 1H), 7.70 (d, J = 6.8 Hz, 1H), 7.60−7.58 (m, 2H), 7.53−7.50 (m, 3H), 7.45 (d, J = 8.2 Hz, 1H), 7.27−7.23 (m, 2H), 7.20−7.14 (m, 2H), 7.07−6.91 (m, 2H), 6.67 (s, 1H), 6.44 (d, J = 7.8 Hz, 1H), 2.62 (q, J = 7.3 Hz, 2H), 2.49 (s, 3H), 1.19 (d, J = 7.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.6, 139.4, 138.4, 137.0, 134.8, 133.6, 131.6, 130.1, 129.6, 129.5, 128.2, 127.6, 127.3, 127.0, 126.8, 126.4, 123.4, 119.8, 118.9, 118.2, 114.7, 111.0, 110.4, 104.2, 94.6, 28.5, 21.6, 15.6; HRMS Calcd for $C_{31}H_{25}N$ (M + H$^+$) 411.1987, found 411.1986.

*6-(p-Tolyl)-10-(p-methoxyphenyl)indolo[2,1-a]isoquinoline (**11j**).* The product was obtained as yellow needles (140.5 mg, 68% yield): mp 150−151 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.22 (d, J = 7.2 Hz, 1H), 7.93 (s, 1H), 7.57 (d, J = 7.8 Hz, 2H), 7.50−7.41 (m, 6H), 7.34 (d, J =

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15.0 Hz, 2H), 7.12 (d, J = 8.4 Hz, 1H), 6.97 (d, J = 6.9 Hz, 2H), 6.53−6.47 (m, 2H), 3.85 (s, 3H), 2.45 (s, 3H).); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.7, 138.8, 138.5, 136.9, 136.3, 134.6, 134.5, 131.4, 130.1, 129.9, 129.1, 128.8, 128.3, 127.6, 127.1, 126.4, 125.3, 123.4, 119.6, 117.9, 114.7, 114.1, 110.8, 94.5, 55.3, 21.5; HRMS Calcd for $C_{30}H_{23}NO$ (M + H^+) 413.1780, found 413.1779.

*6-(4-Butylphenyl)-10-(4-methoxyphenyl)indolo[2,1-a]-isoquinoline (**11k**).* The product was obtained as yellow needles (166.1 mg, 73% yield): mp 78−80 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.21 (d, J = 7.5 Hz, 1H), 7.93 (d, J = 1.2 Hz, 1H), 7.79 (s, 1H), 7.58−7.46 (m, 7H), 7.41−7.37 (m, 4H), 7.19−7.07 (m, 2H), 6.97−6.92 (m, 2H), 6.53−6.49 (m, 1H), 3.84 (s, 5H), 2.84 (q, J = 7.5 Hz, 2H), 1.38 (t, J = 3.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.7, 145.7, 138.4, 137.0, 134.6, 134.5, 133.8, 131.4, 130.1, 129.3, 129.1, 128.4, 128.3, 127.6, 127.0, 126.4, 125.3, 123.4, 119.6, 117.8, 114.7, 114.1, 110.9, 94.5, 55.3, 29.7, 28.7, 15.5; HRMS Calcd for $C_{33}H_{29}NO$ (M + H^+) 455.2249, found 455.2250.

*6-(Biphenyl-4-yl)-10-(4-methoxyphenyl)indolo[2,1-a]isoquinoline (**11l**).* The product was obtained as white needles (154.4 mg, 65% yield): mp 154−155 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.24 (d, J = 7.5 Hz, 1H), 7.95 (s, 1H), 7.77 (dd, J = 7.5 and 9.3 Hz, 4H), 7.66 (d, J = 8.1 Hz, 2H), 7.55 (dd, J = 7.5 and 9.0 Hz, 6H), 7.45−7.39 (m, 3H), 7.13 (d, J = 8.7 Hz, 1H), 6.96 (d, J = 9.0 Hz, 2H), 6.66−6.59 (m, 2H), 3.84 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.7, 142.1, 140.3, 138.0, 137.0, 135.3, 134.6, 131.4, 130.2, 129.8, 129.0, 128.3, 127.9, 127.6, 127.5, 127.2, 126.5, 125.4, 123.4, 119.7, 117.9, 114.7, 111.3, 94.7, 55.3; HRMS Calcd for $C_{35}H_{25}NO$ (M + H^+) 475.1936, found 475.1939.

*6-(p-Ethylphenyl)-10-(p-methoxyphenyl)indolo[2,1-a]-isoquinoline (**11m**).* The product was obtained as yellow needles (149.5 mg, 70% yield): mp 58−60 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.22 (d, J = 7.5 Hz, 1H), 7.93 (d, J = 1.2 Hz, 1H), 7.58−7.52 (m, 3H), 7.50−7.47 (m, 3H), 7.47−7.37 (m, 3H), 7.12 (dd, J = 1.8 and 6.9 Hz, 1H), 7.00−6.94 (m, 3H), 6.53−6.49 (m, 2H), 3.86 (s, 3H), 2.82 (q, J = 7.5 Hz, 2H), 1.37 (t, J = 7.5 Hz, 3H); ^{13}C NMR (100 MHz, DMSO) δ 158.4, 145.3, 133.2, 130.8, 129.8, 129.1, 128.5, 127.8, 126.6, 123.5, 117.3, 114.3, 110.7, 95.0, 55.1, 28.2, 15.6; HRMS Calcd for $C_{31}H_{25}NO$ (M + H^+) 427.1936, found 427.1937.

*6-(m-Methoxyphenyl)-10-(p-methoxyphenyl)indolo[2,1-a]-isoquinoline (**11n**).* The product was obtained as yellow needles (135.2 mg, 63% yield): mp 61−63 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.22 (d, J = 7.5 Hz, 1H), 7.93 (s, 1H), 7.58−7.46 (m, 6H), 7.38 (s, 1H), 7.19−7.13 (m, 3H), 6.96 (d, J = 9.0 Hz, 3H), 6.54 (d, J = 10.5 Hz, 2H), 3.85 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.0, 158.7, 138.1, 137.6, 136.9, 134.6, 131.3, 130.1, 128.9, 128.3, 127.6, 127.2, 126.5, 125.4, 123.4, 121.7, 119.8, 117.8, 115.5, 114.7, 114.5, 114.1, 110.8, 94.6, 55.5, 55.3; HRMS Calcd for $C_{30}H_{23}NO_2$ (M + H^+) 429.1729, found 429.1730.

*6-(p-Phenoxyphenyl)-10-(p-methoxyphenyl)indolo[2,1-a]-isoquinoline (**11o**).* The product was obtained as yellow needles (142.4 mg, 58% yield): mp 171−173 °C; ^{1}H NMR (400 MHz, DMSO) δ 8.34 (d, J = 7.6 Hz, 1H), 7.96 (d, J = 1.8 Hz, 1H), 7.70 (d, J = 6.4 Hz, 1H), 7.62 (d, J = 8.8 Hz, 3H), 7.56−7.46 (m, 5H), 7.23−7.19 (m, 7H), 6.99 (d, J = 9.6 Hz, 2H), 6.71 (s, 1H), 6.49 (d, J = 8.37 Hz, 1H), 3.77 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 158.4, 157.9, 155.9, 137.2, 136.4, 134.4, 133.5, 131.0, 130.7, 130.5, 130.3, 130.2, 129.8, 128.5, 127.9, 127.8, 127.5, 126.6, 124.1, 119.3, 119.2, 118.6, 114.3, 114.2, 110.8, 94.9, 55.1; HRMS Calcd for $C_{35}H_{25}NO_2$ (M + H^+) 491.1885, found 491.1886.

*5-(6-Methoxynaphthlen-2-yl)pyrrolo[2,1-a]isoquinoline (**12a**).* The product was obtained as yellow needles (111.5 mg, 69% yield): mp 116−118 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.07 (d, J = 9.0 Hz, 2H), 7.82 (dd, J = 9.0 and 9.9 Hz, 2H), 7.69 (d, J = 8.1 Hz, 1H), 7.57 (d, J = 7.5 Hz, 1H), 7.48−7.44 (m, 1H), 7.35 (d, J = 7.5 Hz, 1H), 7.31 (s, 1H), 7.24−7.21 (m, 2H), 7.08−7.07 (m, 1H), 6.77 (s, 1H), 6.70 (s, 1H), 3.97 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.5, 136.7, 134.8, 130.9, 129.8, 128.9, 128.1, 127.4, 127.3, 127.1, 126.8, 126.7, 125.8, 125.6, 121.9, 119.5, 114.2, 111.6, 111.5, 105.8, 100.4, 55.4; HRMS Calcd for $C_{23}H_{17}NO$ (M + H^+) 323.1310, found 323.1311.

*5-(Biphenyl-4-yl)pyrrolo[2,1-a]isoquinoline (**12b**).* The product was obtained as yellow needles (113.3 mg, 71% yield): mp 177−179 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.99 (d, J = 8.1 Hz, 1H), 7.67 (s, 4H), 7.60 (d, J = 7.5 Hz, 2H), 7.50 (d, J = 7.8 Hz, 1H), 7.45−7.39 (m, 3H), 7.37−7.30 (m, 1H), 7.30−7.28 (m, 1H), 7.18 (s, 1H), 7.00 (d, J = 1.8 Hz, 1H), 6.65 (d, J = 4.2 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.0, 139.3, 135.3, 133.2, 129.9, 128.2, 127.9, 127.7, 126.6, 126.3, 126.2, 126.1, 125.9, 125.8, 124.7, 124.6, 120.9, 113.1, 110.5, 99.4; HRMS Calcd for $C_{24}H_{17}N$ (M + H^+) 319.1361, found 319.1361.

*5-(4-Ethylphenyl)pyrrolo[2,1-a]isoquinoline (**12c**).* The product was obtained as yellow needles (101.7 mg, 75% yield): mp 68−80 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.04 (d, J = 7.8 Hz, 1H), 7.58−7.53 (m, 3H), 7.47−7.41 (m, 1H), 7.35 (d, J = 8.1 Hz, 3H), 7.47−7.41 (m, 1H), 7.05−7.03 (m, 1H), 6.67 (dd, J = 3.0 and 3.6 Hz, 2H), 2.76 (q, J = 7.5 Hz, 2H), 1.34 (t, J = 5.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.5, 136.7, 132.6, 130.9, 128.8, 128.3, 127.9, 127.4, 127.0, 126.7, 125.7, 125.5, 123.3, 121.9, 114.2, 111.4, 100.3, 28.8, 15.5; HRMS Calcd for $C_{20}H_{17}N$ (M + H^+) 271.1361, found 271.1362.

*5-(p-tert-Butylphenyl)pyrrolo[2,1-a]isoquinoline (**12d**).* The product was obtained as yellow needles (109.2 mg, 73% yield): mp 70−72 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.06 (d, J = 8.1 Hz, 1H), 7.61−7.52 (m, 5H), 7.44 (t, J = 1.2 Hz, 1H), 7.35−7.30 (m, 2H), 7.05 (dd, J = 1.5 and 2.4 Hz, 1H), 6.69−7.04 (m, 2H), 1.42 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.4, 136.7, 132.4, 130.8, 128.5, 127.4, 126.9, 126.8, 125.7, 125.5, 118.6, 114.2, 111.4, 111.3, 108.9, 100.3, 34.7, 31.5; HRMS Calcd for $C_{22}H_{21}N$ (M + H^+) 299.1674, found 299.1674.

General Procedure for the Synthesis of Naphthyridines 14a−f. An oven-dried Schlenk tube with a Teflon screw valve was charged with CuI (10 mol %), **L** (20 mol %), 0.5 mmol of the *N*-heterocycle **3**, 1.1 equiv of 2-haloarylalkyne **8** and KO*t*-Bu (1.4 equiv). The Schlenk tube was capped with a rubber septum and then evacuated and backfilled with nitrogen, followed by DMSO (2.0 mL) added by syringe, through the septum. The septum was then replaced with a Teflon screw valve, and the Schlenk tube was sealed. The reaction mixture was heated to 110 °C until 2-haloarylalkyne **8** had been completely consumed (as determined by TLC) and was allowed to cool to room temperature. The reaction solution was diluted with ethyl acetate (10 mL) and water (15 mL). Organic layer was concentrated under reduced pressure. The crude material so obtained was purified by flash chromatography on silica gel.

*12-Methyl-6-(4-methylphenyl)indolo[2,1-f][1,6]napthyridine (**14a**).* The product was obtained as yellow needles (119.2 mg, 74% yield): mp 168−170 °C; ^{1}H NMR (400 MHz, DMSO) δ 8.59 (d, J = 5.5 Hz, 2H), 7.76 (d, J = 7.8 Hz, 1H), 7.45−7.38 (m, 5H), 7.20 (t, J = 7.3 Hz, 1H), 6.89−6.83 (m, 1H), 6.51 (s, 1H), 6.33 (d, J = 8.7 Hz, 1H), 2.76 (s, 3H), 2.45 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$+DMSO) δ 148.0, 147.0, 141.9, 139.1, 132.6, 130.8, 129.4, 128.3, 122.0, 121.3, 121.2, 120.7, 118.0, 113.8, 111.3, 107.1, 21.0, 11.0; HRMS Calcd for $C_{23}H_{18}N_2$ (M + H^+) 322.1470, found 322.1470.

*12-Methyl-6-(4-ethylphenyl)indolo[2,1-f][1,6]napthyridine (**14b**).* The product was obtained as yellow needles (121.0 mg, 72% yield): mp 118−119 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.67−8.54 (m, 2H), 7.81 (d, J = 9 Hz, 1H), 7.48 (d, J = 7.8 Hz, 2H), 7.41−7.37 (m, 3H), 7.33−7.29 (m, 1H), 6.95 (t, J = 8.4 Hz, 1H), 6.69 (s, 1H), 6.44 (d, J = 8.7 Hz, 1H), 2.85−2.81(m, 5H), 1.37 (t, J = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.2, 148.0, 145.9, 142.7, 133.4, 131.2, 130.9, 130.3, 130.1, 128.8, 128.5, 123.1, 121.4, 121.0, 118.1, 114.5, 111.8, 107.6, 28.8, 15.4, 11.6; HRMS Calcd for $C_{24}H_{20}N_2$ (M + H^+) 336.1626, found 336.1625.

*6-(4-Methoxyphenyl)indolo[2,1-f][1,6]napthyridine (**14c**).* The product was obtained as yellow needles (105.3 mg, 65% yield): mp 173−175 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.72−8.65 (m, 1H), 8.44 (d, J = 7.8 Hz, 1H), 8.05 (d, J = 7.5 Hz, 1H), 7.54 (t, J = 8.4 Hz, 2H), 7.37 (d, J = 9.0 Hz, 2H), 7.28−7.23 (m, 1H), 7.09 (d, J = 8.4 Hz, 2H), 7.02 (t, J = 6.0 Hz, 1H), 6.82 (s, 1H), 6.56 (d, J = 8.7 Hz, 1H), 3.87 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.6, 149.6, 144.9, 142.4, 135.3, 132.3, 130.6, 130.3, 129.6, 128.2, 122.0, 121.6, 121.2, 120.8, 120.4, 114.7, 114.5, 114.3, 112.2, 96.2, 55.6; HRMS Calcd for $C_{22}H_{16}N_2O$ (M + H^+) 324.1263, found 324.1263.

*10-Methoxy-6-(4-methoxyphenyl)indolo[2,1-f][1,6]napthyridine (**14d**).* The product was obtained as yellow needles (122.2 mg, 69% yield): mp 184−185 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.70 (d, J = 3.3 Hz, 1H), 8.43 (d, J = 7.8 Hz, 1H), 7.50 (d, J = 8.7 Hz, 2H), 7.36 (dd, J = 4.8 and 3.3 Hz, 1H), 7.30−7.20 (m, 1H), 7.18 (d, J = 2.4 Hz, 1H), 7.09 (d, J = 8.7 Hz, 2H), 6.73 (s, 1H), 6.61 (dd, J = 2.4 and 6.9 Hz, 1H), 6.43 (d, J = 9.3 Hz, 1H), 3.95 (s, 3H), 3.86 (s, 3H); ^{13}C NMR (100 MHz,

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$CDCl_3$) δ 160.6, 155.4, 149.5, 146.9, 142.2, 135.8, 130.6, 130.4, 128.1, 127.5, 121.5, 120.9, 115.6, 114.4, 111.7, 111.3, 101.1, 95.8, 55.6, 55.5; HRMS Calcd for $C_{23}H_{18}N_2O_2$ (M + H^+) 354.1368, found 354.1368.

*10-Methoxy-6-(thiophen-3-yl)indolo[2,1-f][1,6]napthyridine (**14e**).* The product was obtained as yellow needles (115.5 mg, 70% yield): mp 138−140 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.69 (d, J = 3.3 Hz, 1H), 8.40 (d, J = 7.8 Hz, 1H), 7.62−7.55 (m, 2H), 7.39−7.34 (m, 1H), 7.29 (s, 2H), 7.18 (s, 1H), 6.81 (s, 1H), 6.67 (d, J = 9.3 Hz, 1H), 6.45 (d, J = 9.0 Hz, 1H), 3.87 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.5, 149.5, 146.6, 137.3, 135.9, 135.7, 130.5, 130.4, 128.4, 127.4, 126.8, 125.9, 121.6, 121.1, 115.0, 112.1, 111.6, 101.1, 95.8, 55.6; HRMS Calcd for $C_{20}H_{14}N_2OS$ (M + H^+) 330.0827, found 330.0827.

*6-(p-Methylphenyl)pyrrolo[2,1-f][1,6]naphthyridine (**14f**).* The product was obtained as yellow needles (99.3 mg, 73% yield): mp 110−112 °C; ^{1}H NMR (400 MHz, DMSO) δ 8.61 (d, J = 5.9 Hz, 1H), 8.51 (d, J = 7.8 Hz, 1H), 7.62 (d, J = 8.2 Hz, 2H), 7.47−7.41 (m, 3H), 7.30−7.27 (m, 2H), 6.82 (s, 1H), 6.75−6.74 (m, 1H), 2.69 (q, J = 7.8 Hz, 2H), 1.24 (t, J = 7.8 Hz, 3H); ^{13}C NMR (100 MHz, DMSO) δ 148.1, 145.6, 144.3, 140.0, 131.3, 129.4, 129.0, 128.5, 128.4, 123.1, 122.2, 120.7, 114.4, 112.6, 111.7, 109.4, 102.9, 28.0, 15.3; HRMS Calcd for $C_{19}H_{16}N_2$ (M + H^+) 272.1313, found 272.1313.

General Procedure for the Synthesis of Isoquinoline 15a−g, 16a. An oven-dried Schlenk tube with a Teflon screw valve was charged with CuI (10 mol %), **L** (20 mol %), 0.5 mmol of the *N*-heterocycle **3**, 0.5 equiv of dihaloarylalkyne **10** and base KO*t*-Bu (3.0 equiv). The Schlenk tube was capped with a rubber septum and then evacuated and backfilled with nitrogen, followed by DMSO (2.0 mL) added by syringe, through the septum. The septum was then replaced with a Teflon screw valve, and the Schlenk tube was sealed. The reaction mixture was heated to 110 °C until 2-haloarylalkyne **10** had been completely consumed (as determined by TLC) and was allowed to cool to room temperature. The reaction solution was diluted with ethyl acetate (10 mL) and water (15 mL). Organic layer was concentrated under reduced pressure. The crude material so obtained was purified by flash chromatography on silica gel.

*2,11-Bis(4-ethylphenyl)-8,17-dimethylbenzo[2,3]indolizino[8,7-g]indolo[2,1-a]isoquinoline (**15a**).* The product was obtained as yellow needles (145.1 mg, 49% yield): mp 174−175 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50 (d, J = 7.8 Hz, 2H), 7.23−7.20 (m, 2H), 7.10−6.99 (m, 7H), 7.29 (d, J = 7.2 Hz, 2H), 6.95−6.89 (m, 2H), 6.66 (s, 1H), 6.63 (d, J = 7.8 Hz, 2H), 6.55 (d, J = 0.1 Hz, 1H), 6.20 (s, 1H), 2.60 (q, J = 7.5 Hz, 4H), 2.30 (s, 6H), 1.22−1.10 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.9, 139.9, 138.0, 137.9, 135.9, 135.8, 134.8, 133.9, 133.0, 131.5, 131.2, 129.4, 129.0, 128.6, 127.2, 126.0, 125.0, 124.5, 121.7, 121.3, 121.2, 118.8, 118.7, 118.0, 117.8, 117.2, 112.8, 112.0, 110.6, 27.8, 27.6, 14.5, 14.3, 8.7, 8.6; HRMS Calcd for $C_{44}H_{36}N_2$ (M + H^+) 592.2878, found 592.2874.

*2,11-Bis(4-butylphenyl)-8,17-dimethylbenzo[2,3]indolizino[8,7-g]indolo[2,1-a]isoquinoline (**15b**).* The product was obtained as yellow needles (149.1 mg, 46% yield): mp 189−191 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.64 (s, 1H),7.50 (d, J = 8.1 Hz, 1H), 7.42−7.32 (m, 3H), 7.28−7.17 (m, 3H), 6.99 (m, 7H), 6.96−6.89 (m, 1H), 6.87 (s, 1H), 6.71 (d, J = 8.1 Hz, 1H), 6.61 (s, 1H), 6.30 (s, 1H), 2.60−2.50 (m, 4H), 2.27 (s, 6H), 1.59−1.49 (m, 4H), 1.35−1.25 (m, 4H), 0.94−0.89 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.9, 143.2, 138.8, 135.5, 134.9, 134.8, 134.1, 133.1, 131.3, 130.6, 129.0, 128.7, 128.0, 127.8, 127.5, 126.1, 124.4, 124.3, 122.7, 121.4, 118.9, 118.6, 118.2, 117.9, 113.1, 110.6, 34.6, 34.4, 32.4, 32.3, 28.7, 21.3, 21.1, 12.9(2C), 8.6; HRMS Calcd for $C_{48}H_{44}N_2$ (M + H^+) 648.3504, found 648.3504

*2,11-Bis(4-(tert-butyl)phenyl)benzo[2,3]indolizino[8,7-g]indolo-[2,1-a]isoquinoline (**15c**).* The product was obtained as yellow needles (139.6 mg, 45% yield): mp 214−215 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.84−8.80 (m, 2H), 8.6 (s, 1H), 7.89 (s, 1H), 7.80 (t, J = 8.8 Hz, 2H), 7.60−7.53 (m, 6H), 7.43−7.41 (m, 2H), 7.25−7.18 (m, 4H), 6.93 (t, J = 7.3 Hz, 1H), 6.81 (d, J = 3.7 Hz, 2H), 6.52 (d, J = 8.0 Hz, 1H), 1.55 (s, 9H), 1.49 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.0, 138.0, 135.7, 134.5, 133.4, 132.9, 130.8, 130.5, 129.8, 129.5, 128.9, 128.6, 128.4, 127.7, 125.7, 125.1, 124.1, 122.6, 122.2, 121.6, 120.9, 120.7, 120.5, 120.1, 119.6, 118.8, 116.1, 114.5, 111.5, 111.1, 102.9, 96.5, 35.3, 34.9, 31.4; HRMS Calcd for $C_{46}H_{40}N_2$ (M + H^+) 620.3191, found 620.3189.

*5,12-Di(thiophen-3-yl)indolizino[8,7-g]pyrrolo[2,1-a]isoquinoline (**15d**).* The product was obtained as yellow needles (119.7 mg, 57% yield): mp 242−244 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (s, 2H), 7.71−7.69 (m, 2H), 7.52−7.50 (m, 2H),7.46−7.45 (m, 2H), 7.41−7.38 (m, 2H), 7.10−7.09 (m, 2H), 6.80 (s, 2H), 6.71 (t, J = 2.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.7, 132.2, 130.6, 127.7, 127.1, 127.0, 126.5, 125.3, 123.9, 119.0, 114.7, 111.5, 101.1; HRMS Calcd for $C_{26}H_{16}N_2S_2$ (M + H^+) 420.0755, found 420.0755.

*5,12-Bis(4-butylphenyl)indolizino[8,7-g]pyrrolo[2,1-a]-isoquinoline (**15e**).* The product was obtained as yellow needles (153.5 mg, 59% yield): mp 206−208 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (s, 2H), 7.52 (d, J = 8.1 Hz, 4H), 7.27 (d, J = 8.1 Hz, 4H), 7.22−7.21 (m, 2H), 7.02−7.00 (m, 2H), 6.71 (s, 2H), 6.60 (t, J = 2.9 Hz, 2H), 2.64 (t, J = 7.3 Hz, 4H), 1.65−1.57 (m, 4H), 1.40−1.31 (m, 4H), 0.90 (t, J = 8.1 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.2, 136.9, 132.5, 130.6, 128.8, 128.7, 127.2, 123.9, 118.9, 114.7, 111.3, 111.2, 101.0, 35.5, 33.5, 22.4, 14.0; HRMS Calcd for $C_{38}H_{36}N_2$ (M + H^+) 520.2878, found 520.2879.

*5,12-Bis(4-tert-butylphenyl)indolizino[8,7-g]pyrrolo[2,1-a]-isoquinoline (**15f**).* The product was obtained as yellow needles (150.9 mg, 58% yield): mp 212−214 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (s, 2H), 7.63 (d, J = 8.1 Hz, 4H), 7.55 (d, J = 8.1 Hz, 4H), 7.31−7.21 (m, 2H), 7.09 (dd, J = 2.7 and 1.6 Hz, 2H), 6.80 (s, 2H), 6.67 (t, J = 3.7 Hz, 1H), 1.41 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.4, 136.9, 132.3, 130.6, 128.5, 127.2, 125.8, 124.9, 119.0, 114.9, 111.2, 101.0, 34.8, 31.4, 31.3; HRMS Calcd for $C_{38}H_{36}N_2$ (M + H^+) 520.2878, found 520.2878.

*5,12-Di-p-tolylindolizino[8,7-g]pyrrolo[2,1-a]isoquinoline (**15g**).* The product was obtained as yellow needles (115.6 mg, 53% yield): mp 235−237 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.2 (s, 2H), 7.57 (d, J = 8.0 Hz, 4H), 7.33 (d, J = 8.0 Hz, 4H), 7.27−7.26 (m, 2H), 7.09−7.08 (m, 2H), 6.77 (s, 2H), 6.67 (t, J = 3.6 Hz, 2H), 2.47 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.2, 136.9, 132.4, 130.6, 129.6, 129.5, 128.7, 127.2, 124.1, 123.9, 123.2, 122.8, 122.7, 120.6, 120.3, 118.9, 115.4, 114.7, 111.5, 111.3, 111.2, 108.9, 102.3, 100.9, 21.4; HRMS Calcd for $C_{32}H_{24}N_2$ (M + H^+) 436.1939, found 436.1940.

*3-Bromo-6-(4-ethylphenyl)-2-((4-ethylphenyl)ethynyl)-12-methylindolo[2,1-a]isoquinoline (**16**).* The product was obtained as yellow needles (78.5 mg, 29% yield): mp 167−168 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.67 (s, 1H), 7.57 (d, J = 7.2 Hz, 1H), 7.40 (d, J = 6.9 Hz, 2H), 7.29 (d, J = 7.2 Hz, 2H), 7.21−7.11 (m, 4H), 7.10−7.00 (m, 1H), 6.94 (s, 1H), 6.78 (d, J = 7.8 Hz, 1H), 6.68 (s, 1H), 6.34 (s, 1H), 2.70−2.63 (m, 4H), 2.33 (s, 3H), 1.27−1.20 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 146.2, 145.5, 139.8, 136.5, 135.9, 135.8, 135.2, 132.3, 131.7, 129.7, 128.3, 128.0, 127.3, 125.5, 125.3, 123.8, 122.5, 120.0, 119.6, 119.2, 119.0, 114.2, 111.7, 28.9, 28.7, 15.4, 15.3, 9.7; HRMS Calcd for $C_{35}H_{28}BrN$ (M + H^+) 541.1405, found 541.1406.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Experimental procedures and copies of HRMS, ^{1}H and ^{13}C NMR spectra for all new compounds. CIF for compound **12b** (CCDC 871576). 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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