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Synthesis of highly substituted dihydropyrrolophenanthridine derivatives by tandem reaction

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ABSTRACT

The efficient cross-coupling of bromo(iso)quinoline to 1,6-diynes with the Pd-catalyzed system was established. Using unactivated simple diynes with bromo(iso)quinoline in the presence of palladium catalytic system afforded different kinds of rare 7,11-diphenyl-9,10-dihydro-8*H*-pyrrolo[3,4-*j*]phenanthridine derivatives through regioselective C–H functionalization in one step. Different diynes (**a**–**p**) and different bromo(iso)quinolines were shown to be very active in the reaction. Thus, the generality of this process makes the reaction highly valuable in view of the synthetic and medicinal importance of these pyrrolo[3,4-*j*]phenanthridine derivatives.

1. Introduction

The pyrrolophenanthridine class of substances displays a variety of pharmacological properties. This class has been the subject of considerable interest as potential antitumor, antimicrobial, and antiviral agents.[1] A large number of naturally occurring alkaloids that contain a phenanthridine ring system and have a known scope of activity are mentioned in the literature.[2–4] Lycorine is a phyrrolophenanthridine alkaloid, which displays an antiviral effect against poliovirus and measles and a high antiretroviral activity as well.[5] Therefore, numerous synthetic strategies for the preparation of these scaffolds have been developed.[6–8] Recently, Yu reported the intermolecular C–H functionalization of pyridine rings at the 3- and 4-positions using a Pd^0/PR_3/ArBr catalytic system, providing a powerful method for the preparation of structure-related nicotinic and isonicotinic acids that are of great importance in drug discovery.[9,10] Lautens et al. reported a new and general strategy for the synthesis of hexahydrobenzo[*c*]phenanthridine alkaloids with the novel and highly enantioselective palladium(II)-catalyzed ring-opening reaction of a mesoazabicycle, with an aryl boronic acid as the key step.[11] Cronin developed facile routes for the synthesis and isolation of biologically active DNA intercalating framework tetrahydroimidazo[1,2-*f*]phenanthridines and pyrrolo[1,2-*f*]phenanthridine, which are reactive intermediates in the three-step cascade synthesis of 2,3-dihydro-1*H*-imidazo[1,2-*f*]phenanthridinium cations.[12] Our group has also employed a domino strategy[13] to devise alternative processes for the efficient construction of fused phenanthridine derivatives.[14]

2. Results and discussion

In this study, we introduce a diversity-oriented synthesis of highly substituted dihydropyrrolophenanthridine four-rings condensed ring system from 1,6-diynes and bromoquinoline. The cascade consists of inter-intramolecular Heck reactions and subsequent regioselectively directed arylation by C–H activation of the quinoline ring at the 2- or 4-positions. Herein, we report on the palladium-catalyzed novel domino reactions of **1a**–**p** with 3-bromo(iso)quinoline or 3-bromopyridine to provide a direct, efficient, and economic methodology for the construction of phenanthridine and quinoline through both C–C bond coupling and C–H bond activation.

In our previous research on palladium-catalyzed cyclization, we designed a substance, *N*,*N*-bis(3-phenylprop-2-yn-1-yl)-4-methylbenzenesulfonamide. A survey of the reaction conditions using 3-bromoquinoline (**2a**) and *N*,*N*-bis(3-(4-chlorophenyl)prop-2-yn-1-yl)-4-methylbenzenesulfonamide (**1b**) was performed as a test experiment (Scheme1, Table 1). In a typical experiment, the reaction of **1b** and **2a** in *N*,*N*-dimethylformamide (DMF) in the presence of catalyst $Pd(OAc)_2$ produced 6-chloro-4-(4-chlorophenyl)-2-tosyl-2,3-

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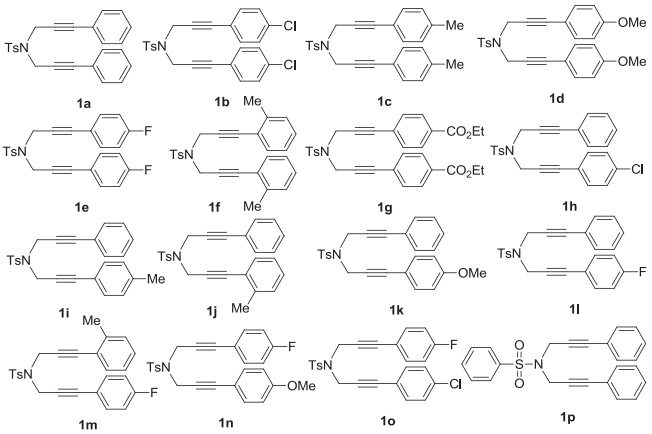
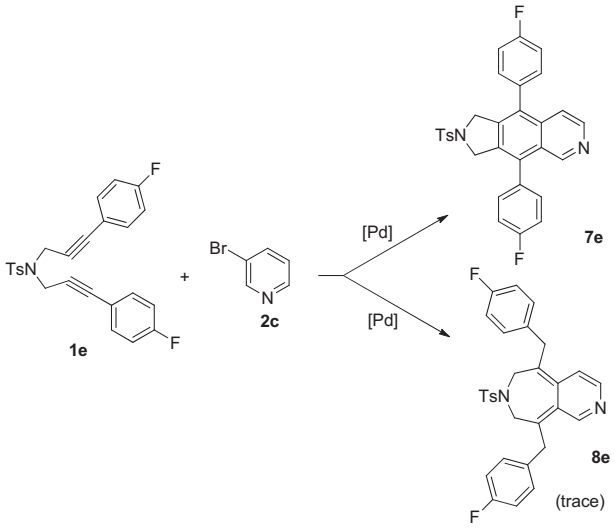


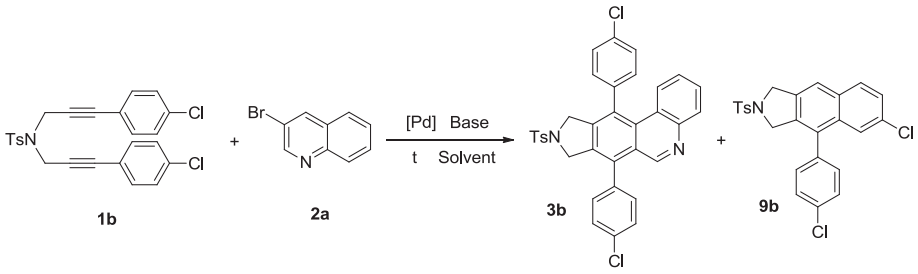


Scheme 1. Synthesis of substituted heterocycle **8e**.

dihydro-1*H*-benzo[*f*]isoindole **9b** in 42% yield after 24 h at 140 °C. By controlling the experimental conditions, we discovered the following: (1) The efficiency of domino reaction to produce the product **3b** can be lowering the reaction temperature to 130 °C (Table 1, entry 6); (2) The additive bases play an important role in the overall efficiency of this domino reaction by simply varying the bases from tributylamine to silver carbonate (Table 1, entries 6, 11–12, 16), with the **3b** in 84%, 15%, and 5% yield when using tributylamine, potassium carbonate, and silver, respectively, under identical conditions; (3) Among the catalysts investigated (Table 1, entries 12–16), the palladium(II) acetate/(triphenylphosphine) catalytic system is most effective (Table 1, entries 6, 13–16). (4) DMF is a better solvent for this reaction than either toluene or MeCN (Table 1, entries 1–2, 7). As shown in Table 1, the tetracyclic compound **3b** is only isolated in yields of 11% and 39%, respectively, when toluene was employed as a solvent, indicating temperature/solvent effects on the outputs of the reactions and on the formation of the final products. Thus, the following standard reaction conditions were used for carrying out the following studies: 1,6-diyne (1 equiv) was reacted with 3-bromoquinoline (1.1 equiv) in the presence of palladium acetate (2 mol %) and Ph_3P (4 mol %), with (n-Bu)$_3$N (1.2 equiv) as an additive in DMF at 130 °C.

To probe the scope of the tandem reaction, a range of substituted 3-bromoquinoline and diynes were examined (Table 2). Various diynes and 3-bromoquinoline or 3-bromoisoquinoline or

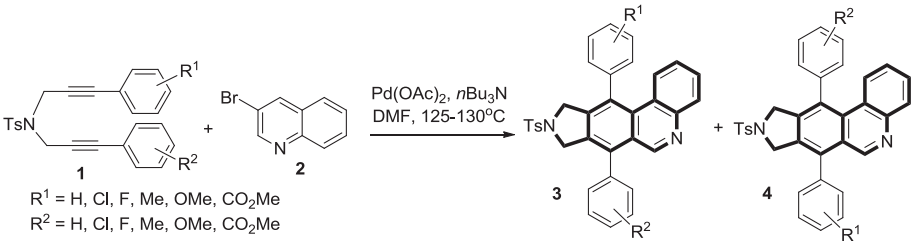
Table 1
Optimization of cyclization conditions[a]

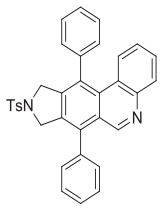


Entry[a]	[Pd]/PPh_3 (mol %)	Base (equiv)	Solvent	t (h)	T[b] (°C)	Yield[c] (%)	
						3b	**9b**
1	$Pd(OAc)_2/PPh_3$ (2:4)	(n-Bu)$_3$N	MeCN	10	100	—	—
2	$Pd(OAc)_2/PPh_3$ (2:4)	(n-Bu)$_3$N	Toluene	10	120	11	Trace
3	$Pd(OAc)_2/PPh_3$ (2:4)	(n-Bu)$_3$N	DMF	11	110	Trace	—
4	$Pd(OAc)_2/PPh_3$ (2:4)	(n-Bu)$_3$N	DMF	11	120	25	7
5	$Pd(OAc)_2/PPh_3$ (2:4)	(n-Bu)$_3$N	DMF	16	130	42	8
6	$Pd(OAc)_2/PPh_3$ (2:4)	(n-Bu)$_3$N	DMF	24	130	84	10
7	$Pd(OAc)_2/PPh_3$ (2:4)	(n-Bu)$_3$N	Toluene	24	130	39	11
8	$Pd(OAc)_2/PPh_3$ (1:2)	(n-Bu)$_3$N	DMF	24	130	54	8
9	$Pd(OAc)_2/PPh_3$ (2:4)	(n-Bu)$_3$N	DMF	15	130	61	9
10	$Pd(OAc)_2/PPh_3$ (2:4)	(n-Bu)$_3$N	DMF	24	140	14	42
11	$Pd(OAc)_2/PPh_3$ (2:4)	K_2CO_3	DMF	24	130	15	—
12	$Pd(OAc)_2/PPh_3$ (2:4)	$NaHCO_3$	DMF	24	130	Trace	—
13	$Pd(PPh_3)_4$ (2)	(n-Bu)$_3$N	DMF	24	130	10	—
14	$PdCl_2$ (2)	(n-Bu)$_3$N	DMF	24	130	—	—
15	$Pd(dba)_2$[d] (2)	(n-Bu)$_3$N	DMF	24	130	20	Trace
16	$Pd(OAc)_2$ (2)	Ag_2CO_3	DMF	24	130	5	—

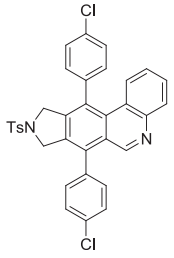
[a] All reactions were carried out under argon using **1b** (1.0 equiv), 3-bromoquinoline (1.1 equiv), [$Pd(OAc)_2$] (2 mol %), Ph_3P, base (2.0 equiv) and solvent (10 mL) at the indicated temperature.
[b] Oil bath temperature.
[c] Isolated yield.
[d] dba: dibenzylidene acetone.

Table 2
The palladium-catalyzed domino reaction for the formation of fused pyrrolophenanthridine[a,b]

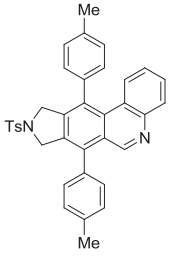




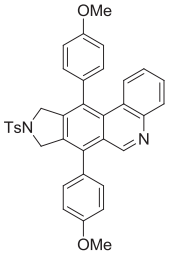
3a (75%)



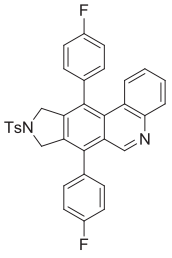
3b (84%)



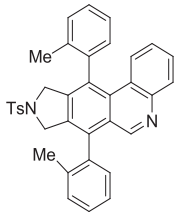
3c (65%)



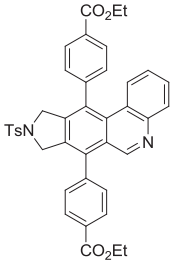
3d (59%)



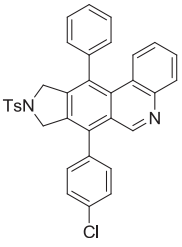
3e (86%)



3f (85%)



3g (56%)



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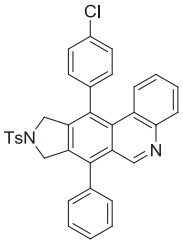
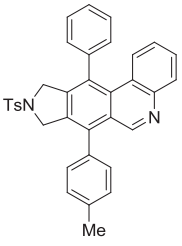
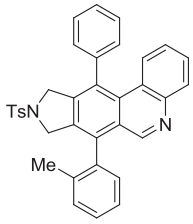


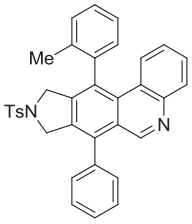
4h (50%)



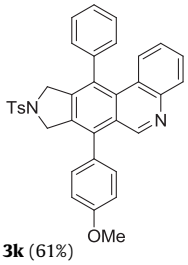
3i (66%)



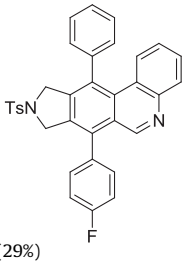
3j (31%)



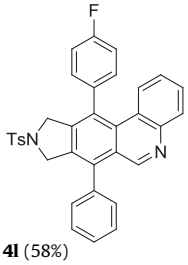
4j (55%)



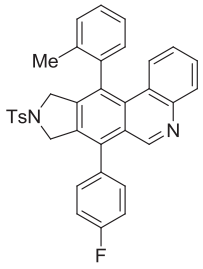
3k (61%)



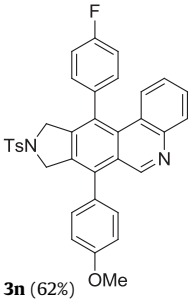
3l (29%)



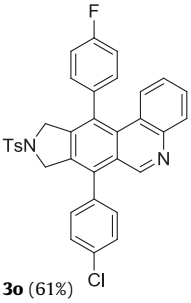
4l (58%)



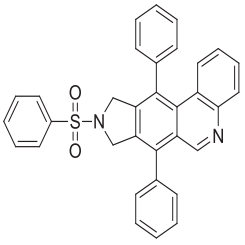
3m (71%)



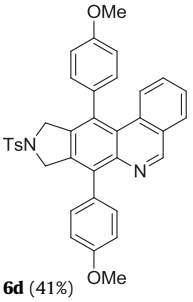
3n (62%)



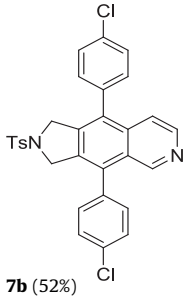
3o (61%)



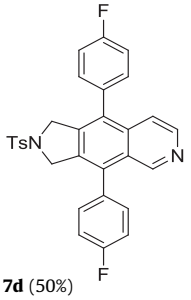
5p (74%)



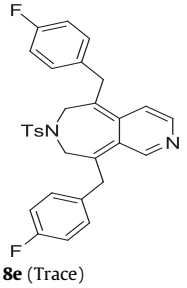
6d (41%)



7b (52%)



7d (50%)



8e (Trace)

[a] Reaction conditions: **a**–**p** (1.0 equiv), bromo(iso)quinoline (1.2 equiv), $Pd(OAc)_2$ (2 mol %), PPh_3 (4 mol %), (n-Bu)$_3$N (1.2 equiv), DMF 10 mL, 125–130 °C, 24 h.
[b] Isolated yield after flash column chromatography.

3-bromopyridine is compatible with this palladium-catalyzed domino reaction. Several 7,11-diphenyl-9,10-dihydro-8*H*-pyrrolo[3,4-*j*]phenanthridine compounds were readily isolated in good to excellent yields, except in the case of **6d**, where 3-bromoisoquinoline was employed. The *para*- or *ortho*- substituted groups on the benzene ring of 1,6-diynes could be chloro, fluoro, methyl, methoxyl, and ethoxycarbonyl. Using 3-bromoquinoline with diyne substrates (**b**, **e**–**f**, **h**, **j**, **l**), the reaction yielded 7,11-diphenyl-9,10-dihydro-8*H*-pyrrolo[3,4-*j*]phenanthridine **3b**, **3e**, **3f**, **3h**+**4h**, **3j**+**4j**, and **3l**+**4l**, respectively, in yields higher than 83%. The yield of compound (**3l**+**4l**) was the highest at 87%. When 3-bromoquinoline was used in the reaction with **a**, **c**,**d**, **g**, **i**, **k**, and **m**–**p**, the desired pyrrolo[3,4-*j*]phenanthridines were obtained in good yields ranging from 56% to 75% (**3a**, **3c**, **3d**, **3g**, **3i**, **3k**, **3m**, **3n**, **3o**, and **5p**). The reaction of 3-bromoquinoline with diyne having a *para*-chloro, *ortho*-methyl, or *para*-fluoro group (**3h**, **3j**, and **3l**) gave much lower yields of the products than that of **4h**, **4j**, and **4l**. Compound **6d** yield was low (41%), but it is a novel 7,11-diphenyl-9,10-dihydro-8*H*-pyrrolo[3,4-*b*]phenanthridine. Finally, with these conditions, the generality of the cyclization was studied using 3-bromopyridine in place of 3-bromoquinoline. Results showed that the 4,9-diphenyl-2-tosyl-2,3-dihydro-1*H*-pyrrolo[3,4-*g*]isoquinolines **7b** and **7e** (Scheme 1) gave moderate yields of 52% and 50%, respectively. We isolated traces of **8e** besides the product **7e** when *N*,*N*-bis(3-(4-fluorophenyl)prop-2-yn-1-yl)-4-methylbenzenesulfonamide and 3-bromopyridine were used in the reaction. The regioselectivity of the reaction has no clear superiority when either election-donating or election-withdrawing groups on the aryl halides. A proposed pathway for this tandem Heck/C–H functionalization reaction is shown in Scheme 1.

All the resulting fused pyrrolo[3,4-*b*]phenanthridine compounds were confirmed by various spectroscopic techniques (^{1}H, ^{13}C NMR, and IR spectroscopy, and HRMS). The molecular structures and relative configurations of **3e** (Fig. 1) and **8e** (Fig. 2) were unambiguously confirmed by single-crystal X-ray analysis (Supplementary data).[15]

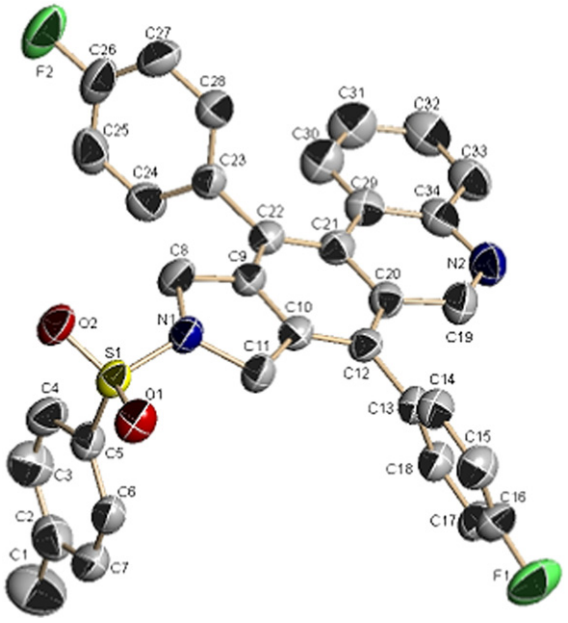


Fig. 1. ORTEP polt of **3e** showing ellipsoids at the 30% probability level. Selected bond lengths [Å] and angles [°]: C9–C10 1.396(5), C10–C12 1.384(5), C12–C20 1.417(5), C21–C22 1.418(5), C9–C22 1.375(5), C9–C10–C11 110.7(3), C11–C10–C12 129.3(3), C10–C12–C20 117.5(3), C9–C22–C21 118.2(3), C12–C20–C21 122.6(3).

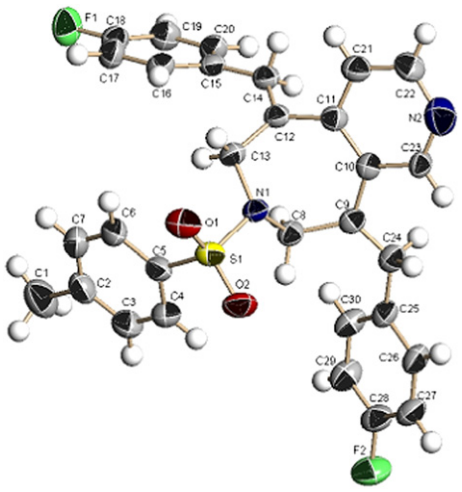
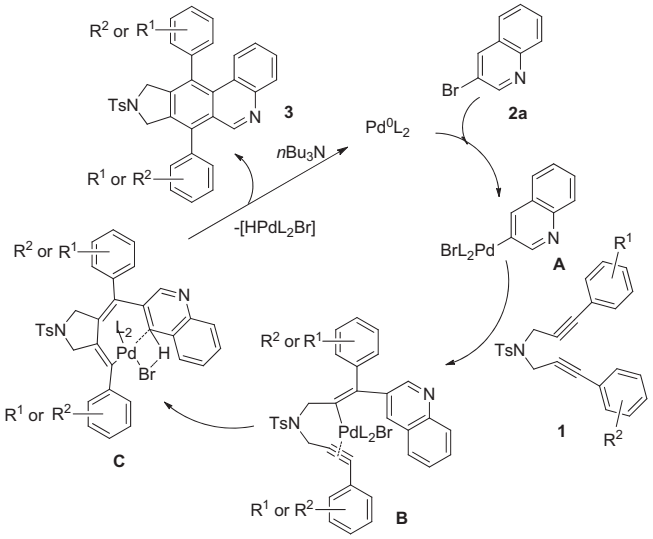


Fig. 2. ORTEP polt of **8e** showing ellipsoids at the 30% probability level. Selected bond lengths [Å] and angles [°]: C9–C10 1.487(3), C9–C24 1.336(3), C10–C11 1.402(3), C11–C12 1.491(3), C12–C14 1.337(3), N1–C8–C9 111.4(2), C8–C9–C10 119.0(2), C9–C10–C11 123.8(2), C10–C11–C12 124.4(2), C11–C12–C13 118.6(2), N1–C13–C12 111.3(2).

Simplified catalytic cycle mechanisms for selective formation pyrrolophenanthridines are proposed in Scheme 2. Oxidative addition of bromoquinoline (**2a**) would yield aryl-palladium intermediate **A**, which can subsequently undergo carbopalladation with the diyne moiety (**1**) to yield intermediate **B**. Intermediate **B** possesses a carbon–carbon double bond that can undergo carbopalladation and σ-bond metathesis onto the aryl group to yield intermediate C. Proton abstraction[16] by the base yields pyrrolophenanthridine **3**.



Scheme 2. Proposed catalytic cycle.

3. Conclusions

We developed a tandem sequence method for the preparation of diversely substituted pyrrolo[3,4-*j*]phenanthridines from readily available precursors through multistep C–C bond formation and C–H activation of quinoline or isoquinoline ring. This series produced pyrrolo[3,4-*j*]phenanthridine derivatives in moderate to very good yields. This methodology will aid in generating more interesting structures for use in biological studies. Aside from the

products, traces of novel pyrido[3,4-*d*]azepine were also dissociated when *N*,*N*-bis(3-(4-fluorophenyl)prop-2-yn-1-yl)-4-methylbenzenesulfonamide and 3-bromopyridine were used in the reaction. Further investigations to understand this catalytic transformation, an evaluation of the process with a broader scope of substrates, and synthesis of more complex π-system heterocycles are in progress.

4. Experimental

4.1. General experiment

All the catalytic reactions were performed under an argon atmosphere using the oven-dried Schlenk flask. Chemicals were purchased from Alfa Aesar and Acros Chemicals. All solvents and materials were dried, distilled, or recrystallized before use. ^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were recorded on a Bruker Avance 300 spectrometer with $CDCl_3$ as the solvent. Chemical shifts (δ) are reported in parts per million by assigning TMS resonance in the ^{1}H NMR spectra as 0.00 ppm and $CDCl_3$ resonance in the ^{13}C spectra as 77.0 ppm. All coupling constants (*J* values) were reported in hertz (Hz). Column chromatography was performed on silica gel 300–400 mesh. Melting points were determined using a Gallenkamp melting point apparatus and are uncorrected. The FT-IR spectra were recorded from KBr pellets or thin film from $CHCl_3$ on the NaCl window in the 4000–400 cm^{-1} ranges on a Nicolet 5DX spectrometer. All HRMS spectra were record using EI at 70 eV. X-ray Crystallography diffraction data of ab was collected at room temperature with a Bruker SMART Apex CCD diffractometer with Mo Kα radiation (λ=0.71073 Å) with a graphite monochromator using the ω-scan mode. Data reductions and absorption corrections were performed with SAINT and SADABS software, respectively.[17] The structure was solved by direct methods and refined on F^2 by full-matrix least squares using SHELXTL.[18] All non-hydrogen atoms were treated anisotropically. The positions of hydrogen atoms were generated geometrically. 1,6-Diynes **a**–**p** were prepared by published procedures.[19]

4.2. Synthesis

Typical procedure for the palladium-catalyzed domino reaction of the 1,6-diynes with bromo(iso)quinoline: diyne **1a**–**p** (1.0 equiv), 3-bromoquinoline (1.2 equiv), $Pd(OAc)_2$ (2 mol %), and PPh_3 (4 mol %) were added to the degassed solution of $(n\text{-}Bu)_3N$ (1.2 equiv) in DMF (5 mL) and the mixture was stirred at room temperature for 40 min then heated at 125–130 °C for 24 h. The reaction mixture was cooled, quenched with water, and extracted with EtOAc (3×5 mL). The combined organic layers were washed with hydrochloric acid (5%), aqueous sodium carbonate (5%), and saturated aqueous sodium chloride solution. After separation, the organic layer was dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash chromatography (6:1 petroleum ether/EtOAc) to give the corresponding product **3**.

*4.2.1. 7,11-Diphenyl-9-tosyl-9,10-dihydro-8H-pyrrolo[3,4-j]phenanthridine (**3a**).* Yellow powder; 395 mg (75%); R_f=0.38 (petroleum ether/EtOAc=4:1); mp 253–254 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ=9.08 (s, 1H; Ar–H), 8.08 (d, *J*=6.9 Hz, 1H; Ar–H), 7.69–7.57 (m, 5H; Ar–H), 7.56–7.47 (m, 5H; Ar–H), 7.31 (m, 6H; Ar–H), 7.14 (s, 1H; Ar–H), 4.62 (s, 2H; –CHH–), 4.51 (s, 2H; –CHH–), 2.40 ppm (s, 3H; CH_3–); ^{13}C NMR (75 MHz, $CDCl_3$): δ=151.5, 143.8, 145.2, 140.4, 139.8, 136.0, 135.9, 134.4, 133.6, 133.3, 130.0, 129.8, 129.4, 128.9, 128.5, 128.4, 128.2, 128.1, 127.5, 126.7, 125.9, 59.6, 53.7, 21.5 ppm; FT-IR (KBr): $\tilde{\nu}_{max}$=3055, 1597, 1448, 1400, 1346, 1317, 1157, 1095, 702, 611, 547 cm^{-1}; HRMS (ESI): *m*/*z* [M+H]$^+$ calcd for $C_{34}H_{27}N_2O_2S$: 527.1794; found: 527.1778.

*4.2.2. 7,11-Bis(4-chlorophenyl)-9-tosyl-9,10-dihydro-8H-pyrrolo[3,4-j]phenanthridine (**3b**).* Yellow powder; 499 mg (84%); R_f=0.36 (petroleum ether/EtOAc=4:1); mp 258–259 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ=9.08 (s, 1H; Ar–H), 8.12 (s, 1H; Ar–H), 7.70–7.58 (m, 7H; Ar–H), 7.31–7.23 (m, 8H; Ar–H), 4.58 (s, 2H; –CHH–), 4.45 (s, 2H; –CHH–), 2.41 ppm (s, 3H; CH_3–); ^{13}C NMR (75 MHz, $CDCl_3$): δ=151.0, 143.9, 139.9, 138.6, 135.0, 134.8, 134.6, 134.2, 133.2, 132.6, 130.7, 130.4, 130.2, 129.9, 129.5, 129.3, 128.5, 127.5, 126.5, 126.3, 54.3, 53.5, 21.5 ppm; FT-IR (KBr): $\tilde{\nu}_{max}$=2360, 1597, 1492, 1340, 1161, 1012, 767, 673, 592, 545, 526 cm^{-1}; HRMS (ESI): *m*/*z* [M+H]$^+$ calcd for $C_{34}H_{25}Cl_2N_2O_2S$: 595.1015; found: 595.1007.

*4.2.3. 7,11-Di-p-tolyl-9-tosyl-9,10-dihydro-8H-pyrrolo[3,4-j]phenanthridine (**3c**).* Yellow powder; 360 mg (65%); R_f=0.42 (petroleum ether/EtOAc=4:1); mp 256–257 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ=9.09 (s, 1H; Ar–H), 8.07 (d, *J*=7.7 Hz, 1H; Ar–H), 7.67 (d, *J*=8.0 Hz, 2H; Ar–H), 7.56 (t, *J*=8.7 Hz, 2H; Ar–H), 7.37 (t, *J*=6.7 Hz, 4H; Ar–H), 7.31–7.21 (m, 4H; Ar–H), 7.16 (d, *J*=7.6 Hz, 3H; Ar–H), 4.60 (s, 2H; –CHH–), 4.49 (s, 2H; –CHH–), 2.54 (s, 3H; CH_3–), 2.50 (s, 3H; CH_3–), 2.39 ppm (s, 3H; CH_3–); ^{13}C NMR (75 MHz, $CDCl_3$): δ=151.7, 145.3, 143.8, 140.0, 138.3, 138.1, 137.5, 136.0, 134.4, 133.4, 133.0, 130.7, 130.0, 129.9, 129.7, 129.4, 128.1, 127.9, 127.5, 126.8, 125.9, 54.6, 53.9, 21.6, 21.5, 21.4 ppm; FT-IR (KBr): $\tilde{\nu}_{max}$=2358, 1597, 1514, 1446, 1346, 1166, 1097, 771, 669, 549 cm^{-1}; HRMS (ESI): *m*/*z* [M+H]$^+$ calcd for $C_{36}H_{31}N_2O_2S$: 555.2107; found: 555.2092.

*4.2.4. 7,11-Bis(4-methoxyphenyl)-9-tosyl-9,10-dihydro-8H-pyrrolo[3,4-j]phenanthridine (**3d**).* Yellow powder; 346 mg (59%); R_f=0.38 (petroleum ether/EtOAc=4:1); mp 253–254 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ=9.05 (s, 1H; Ar–H), 8.08 (s, 1H; Ar–H), 7.69–7.59 (m, 4H; Ar–H), 7.31–7.22 (m, 5H; Ar–H), 7.21–7.07 (m, 6H; Ar–H), 4.61 (s, 2H; –CHH–), 4.50 (s, 2H; –CHH–), 3.96 (d, *J*=9.7 Hz, 6H; CH_3O–), 2.39 ppm (s, 3H; CH_3–); ^{13}C NMR (75 MHz, $CDCl_3$): δ=159.5, 151.5, 149.8, 145.4, 143.7, 140.3, 136.8, 136.0, 134.5, 133.5, 132.5, 130.7, 130.0, 129.8, 129.3, 128.2, 128.0, 127.5, 126.7, 126.1, 115.5, 114.4, 55.4, 54.6, 53.9, 21.5 ppm; FT-IR (KBr): $\tilde{\nu}_{max}$=2835, 1608, 1514, 1340, 1161, 1103, 1031, 767, 669, 546 cm^{-1}; HRMS (ESI): *m*/*z* [M+H]$^+$ calcd for $C_{36}H_{31}N_2O_4S$: 587.2005; found: 587.2002.

*4.2.5. 7,11-Bis(4-fluorophenyl)-9-tosyl-9,10-dihydro-8H-pyrrolo[3,4-j]phenanthridine (**3e**).* Yellow powder; 483 mg (86%); R_f=0.42 (petroleum ether/EtOAc=4:1); mp 246–247 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ=9.11 (s, 1H; Ar–H), 8.07 (d, *J*=8.5 Hz, 1H; Ar–H), 7.71–7.47 (m, 4H; Ar–H), 7.29–7.21 (m, 6H; Ar–H), 7.20–7.16 (m, 5H; Ar–H), 4.58 (d, *J*=11.8 Hz, 2H; –CHH–), 4.48 (d, *J*=11.5 Hz, 2H; –CHH–), 2.38 ppm (d, *J*=17.0 Hz, 3H; CH_3–); ^{13}C NMR (75 MHz, $CDCl_3$): δ=164.5, 164.4, 161.2, 161.1, 151.2, 143.9, 140.2, 136.3, 136.2, 135.2, 134.7, 133.5, 132.8, 131.8, 131.3, 131.2, 130.3, 130.0, 129.9, 128.5, 127.5, 126.5, 126.2, 117.4, 117.1, 116.4, 116.1, 54.4, 53.6, 21.5 ppm; FT-IR (KBr): $\tilde{\nu}_{max}$=2854, 1604, 1512, 1348, 1157, 1095, 815, 667, 548 cm^{-1}; HRMS (ESI): *m*/*z* [M+H]$^+$ calcd for $C_{34}H_{25}F_2N_2O_2S$: 563.1606; found: 563.1587.

*4.2.6. 7,11-Di-o-tolyl-9-tosyl-9,10-dihydro-8H-pyrrolo[3,4-j]phenanthridine (**3f**).* Yellow powder; 471 mg (85%); R_f=0.48 (petroleum ether/EtOAc=4:1); mp 186–187 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ=8.90 (s, 1H; Ar–H), 8.10 (d, *J*=7.8 Hz, 1H; Ar–H), 7.68 (d, *J*=7.3 Hz, 2H; Ar–H), 7.58–7.38 (m, 8H; Ar–H), 7.30 (d, *J*=7.4 Hz, 2H; Ar–H), 7.20 (t, *J*=8.5 Hz, 3H; Ar–H), 4.65–4.31 (m, 4H; –CHH–), 2.39 (s, 3H; CH_3–), 1.98 (s, 3H; CH_3–), 1.90 ppm (s, 3H; CH_3–); ^{13}C NMR (75 MHz, $CDCl_3$): δ=151.6, 145.3, 143.9, 139.8, 135.5, 131.4, 130.6, 130.3, 129.9, 129.3, 129.2, 128.9, 128.4, 128.0, 127.9, 127.7, 127.5, 126.7, 126.5, 125.4, 125.3, 54.6, 53.8, 21.5, 19.9, 19.5 ppm; FT-IR

(KBr): $\tilde{\nu}_{max}$=2918, 1595, 1446, 1344, 1165, 1097, 818, 667, 550 cm^{-1}; HRMS (ESI): *m*/*z* $[M+H]^+$ calcd for $C_{36}H_{31}N_2O_2S$: 555.2107; found: 555.2058.

*4.2.7. Diethyl 4,4′-(9-tosyl-9,10-dihydro-8H-pyrrolo[3,4-j]phenanthridine-7,11-diyl)dibenzoate (**3g**).* Yellow powder; 375 mg (56%); R_f=0.38 (petroleum ether/EtOAc=4:1); mp 217–218 °C; ^1H NMR (300 MHz, $CDCl_3$): δ=9.03 (s, 1H; Ar–H), 8.29 (d, *J*=6.5 Hz, 4H; Ar–H), 8.11 (d, *J*=7.3 Hz, 1H; Ar–H), 7.67–7.49 (m, 6H; Ar–H), 7.48–7.27 (m, 5H; Ar–H), 7.17 (d, *J*=6.8 Hz, 1H; Ar–H), 4.56–4.46 (m, 8H; –CHH–), 2.40 (s, 3H; CH_3–), 1.49 ppm (d, *J*=5.9 Hz, 6H; $-OCH_2CH_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ=166.2, 150.9, 145.5, 145.0, 144.0, 140.6, 139.7, 135.4, 134.5, 133.4, 133.1, 131.3, 130.9, 130.7, 130.3, 130.0, 129.6, 128.6, 128.4, 127.5, 126.6, 126.4, 123.7, 118.5, 61.4, 54.3, 53.5, 21.5, 14.4 ppm; FT-IR (KBr): $\tilde{\nu}_{max}$=2978, 1722, 1709, 1274, 1161, 763, 705, 665 cm^{-1}; HRMS (ESI): *m*/*z* $[M+H]^+$ calcd for $C_{40}H_{35}N_2O_6S$: 671.2217; found: 671.2189.

*4.2.8. 7-(4-Chlorophenyl)-11-phenyl-9-tosyl-9,10-dihydro-8H-pyrrolo[3,4-j]phenanthridine (**3h**).* Yellow powder; 169 mg (33%); R_f=0.42 (petroleum ether/EtOAc=4:1); mp 265–266 °C; ^1H NMR (300 MHz, $CDCl_3$): δ=9.07 (s, 1H; Ar–H), 8.07 (d, *J*=7.8 Hz, 1H; Ar–H), 7.78 (d, *J*=7.2 Hz, 2H; Ar–H), 7.58–7.45 (m, 11H; Ar–H), 7.36–7.26 (m, 4H; Ar–H), 7.13 (t, *J*=7.4 Hz, 1H; Ar–H), 4.63 (s, 2H; –CHH–), 4.52 ppm (s, 2H; –CHH–); ^{13}C NMR (75 MHz, $CDCl_3$): δ=151.6, 145.4, 140.5, 139.7, 136.5, 136.0, 133.7, 132.9, 129.5, 129.3, 129.0, 128.6, 128.5, 128.2, 127.5, 126.8, 126.0, 54.6, 53.8 ppm; FT-IR (KBr): $\tilde{\nu}_{max}$=2310, 1445, 1348, 1168, 1099, 763, 619, 594, 573 cm^{-1}; HRMS (ESI): *m*/*z* $[M+H]^+$ calcd for $C_{33}H_{25}N_2O_2S$: 513.1637; found: 513.1622.

*4.2.9. 11-(4-Chlorophenyl)-7-phenyl-9-tosyl-9,10-dihydro-8H-pyrrolo[3,4-j]phenanthridine (**4h**).* Yellow powder; 280 mg (50%); R_f=0.38 (petroleum ether/EtOAc=4:1); mp 266–267 °C; ^1H NMR (300 MHz, $CDCl_3$): δ=9.07 (s, 1H; Ar–H), 8.09 (d, *J*=7.6 Hz, 1H; Ar–H), 7.68 (d, *J*=7.6 Hz, 2H; Ar–H), 7.60–7.51 (m, 7H; Ar–H), 7.33–7.12 (m, 7H; Ar–H), 4.60 (s, 2H; –CHH–), 4.47 (s, 2H; –CHH–), 2.40 ppm (s, 3H; CH_3–); ^{13}C NMR (75 MHz, $CDCl_3$): δ=151.5, 145.4, 144.0, 140.0, 139.0, 136.5135.9, 134.6, 132.3, 130.4, 130.3, 129.9, 128.7, 128.5, 127.6, 126.6, 126.2, 54.4, 53.7, 21.6 ppm; FT-IR (KBr): $\tilde{\nu}_{max}$=2954, 1595, 1490, 1157, 1093, 831, 765, 588, 523 cm^{-1}; HRMS (ESI): *m*/*z* $[M+H]^+$ calcd for $C_{34}H_{26}ClN_2O_2S$: 561.1404; found: 561.1377.

*4.2.10. 11-Phenyl-7-(p-tolyl)-9-tosyl-9,10-dihydro-8H-pyrrolo[3,4-j]phenanthridine (**3i**).* Yellow powder; 356 mg (66%); R_f=0.46 (petroleum ether/EtOAc=4:1); mp 271–272 °C; ^1H NMR (300 MHz, $CDCl_3$): δ=9.12 (s, 1H; Ar–H), 8.09 (s, 1H; Ar–H), 7.69–7.50 (m, 7H; Ar–H), 7.39–7.13 (m, 9H; Ar–H), 4.62 (s, 2H; –CHH–), 4.51 (s, 2H; –CHH–), 2.52 (s, 3H; CH_3–), 2.40 (s, 3H; CH_3–); ^{13}C NMR (75 MHz, $CDCl_3$): δ=151.7, 145.4, 143.8, 140.5, 139.9, 138.4, 136.4, 134.6, 133.5, 133.0, 130.4, 130.9, 130.1, 129.9, 129.7, 129.4, 128.4, 128.2, 127.6, 126.9, 126.0, 54.6, 53.9, 21.5, 21.4 ppm; FT-IR (KBr): $\tilde{\nu}_{max}$=2866, 1597, 1157, 1095, 759, 594, 522 cm^{-1}; HRMS (ESI): *m*/*z* $[M+H]^+$ calcd for $C_{35}H_{29}N_2O_2S$: 541.1950; found: 541.1944.

*4.2.11. 11-Phenyl-7-(o-tolyl)-9-tosyl-9,10-dihydro-8H-pyrrolo[3,4-j]phenanthridine (**3j**).* Yellow powder; 167 mg (31%); R_f=0.45 (petroleum ether/EtOAc=4:1); mp 157–158 °C; ^1H NMR (300 MHz, $CDCl_3$): δ=8.87 (s, 1H; Ar–H), 8.08 (d, *J*=7.9 Hz, 1H; Ar–H), 7.68 (d, *J*=7.9 Hz, 2H; Ar–H), 7.59 (s, 3H; Ar–H), 7.54–7.27 (m, 9H; Ar–H), 7.15 (t, *J*=9.2 Hz, 2H; Ar–H), 4.60–4.40 (m, 4H; –CHH–), 2.40 (s, 3H; CH_3–), 1.99 (s, 3H; CH_3–); ^{13}C NMR (75 MHz, $CDCl_3$): δ=151.4, 145.5, 143.8, 140.5, 140.0, 136.2, 135.4, 134.5, 133.7, 130.6, 130.2, 130.1, 129.8, 129.3, 128.9, 128.4, 128.2, 127.5, 126.8, 126.6, 126.0, 124.3, 54.6, 53.7, 21.5, 19.9 ppm; FT-IR (KBr): $\tilde{\nu}_{max}$=3057, 1344, 1157, 1095, 771, 705, 671, 590, 549 cm^{-1}; HRMS (ESI): *m*/*z* $[M+H]^+$ calcd for $C_{35}H_{29}N_2O_2S$: 541.1950.; found: 541.1926.

*4.2.12. 7-Phenyl-11-(o-tolyl)-9-tosyl-9,10-dihydro-8H-pyrrolo[3,4-j]phenanthridine (**4j**).* Yellow powder; 297 mg (55%); R_f=0.43 (petroleum ether/EtOAc=4:1); mp 251–252 °C; ^1H NMR (300 MHz, $CDCl_3$): δ=9.11 (s, 1H; Ar–H), 8.09 (d, *J*=7.7 Hz, 1H; Ar–H), 7.68 (d, *J*=7.8 Hz, 2H; Ar–H), 7.57 (d, *J*=6.5 Hz, 4H; Ar–H), 7.50–7.27 (m, 8H; Ar–H), 7.16 (d, *J*=6.1 Hz, 2H; Ar–H), 4.71–4.30 (m, 4H; –CHH–), 2.40 (s, 3H; CH_3–), 1.92 (s, 3H; CH_3–); ^{13}C NMR (75 MHz, $CDCl_3$): δ=151.8, 145.1, 143.8, 139.7, 139.6, 136.1, 136.0, 135.3, 133.6, 131.4, 130.2, 130.0, 129.5, 129.0, 128.9, 128.5, 128.4, 128.0, 127.7, 127.5, 126.7, 125.4, 124.5, 54.5, 53.9, 21.5, 19.6 ppm; FT-IR (KBr): $\tilde{\nu}_{max}$=3051, 1595, 1167, 1095, 667, 613, 546 cm^{-1}; HRMS (ESI): *m*/*z* $[M+H]^+$ calcd for $C_{35}H_{29}N_2O_2S$: 541.1950; found: 541.1931.

*4.2.13. 7-(4-Methoxyphenyl)-11-phenyl-9-tosyl-9,10-dihydro-8H-pyrrolo[3,4-j]phenanthridine (**3k**).* Yellow powder; 339 mg (61%); R_f=0.39 (petroleum ether/EtOAc=4:1); mp 231–232 °C; ^1H NMR (300 MHz, $CDCl_3$): δ=9.13 (s, 1H; Ar–H), 8.08 (d, *J*=7.6 Hz, 1H; Ar–H), 7.68 (d, *J*=7.4 Hz, 2H; Ar–H), 7.58 (s, 4H; Ar–H), 7.48 (d, *J*=8.4 Hz, 1H; Ar–H), 7.29 (s, 6H; Ar–H), 7.20–7.08 (m, 3H; Ar–H), 4.63 (s, 2H; –CHH–), 4.50 (s, 2H; –CHH–), 3.95 (s, 3H; CH_3O–), 2.40 (s, 3H; CH_3–); ^{13}C NMR (75 MHz, $CDCl_3$): δ=159.7, 151.7, 145.4, 143.8, 140.5, 139.8, 135.9, 134.7, 133.5, 133.4, 130.7, 130.0, 129.9, 129.5, 129.3, 128.9, 128.4, 128.2, 128.1, 127.5, 126.8, 125.9, 115.5, 114.4, 55.5, 54.6, 53.9, 21.5 ppm; FT-IR (KBr): $\tilde{\nu}_{max}$=3028, 1612, 1514, 1344, 1157, 1095, 810, 594 cm^{-1}; HRMS (ESI): *m*/*z* $[M+H]^+$ calcd for $C_{35}H_{29}N_2O_3S$: 557.1899; found: 557.1883.

*4.2.14. 7-(4-Fluorophenyl)-11-phenyl-9-tosyl-9,10-dihydro-8H-pyrrolo[3,4-j]phenanthridine (**3l**).* Yellow powder; 158 mg (29%); R_f=0.42 (petroleum ether/EtOAc=4:1); mp 262–263 °C; ^1H NMR (300 MHz, $CDCl_3$): δ=9.05 (s, 1H; Ar–H), 8.09 (s, 1H; Ar–H), 7.69–7.50 (m, 7H; Ar–H), 7.31 (s, 8H; Ar–H), 7.15 (s, 1H; Ar–H), 4.60 (s, 2H; –CHH–), 4.50 (s, 2H; –CHH–), 2.40 ppm (s, 3H; CH_3–); ^{13}C NMR (75 MHz, $CDCl_3$): δ=164.5, 161.2, 151.1, 145.4, 143.9, 140.4, 140.0, 135.0, 134.7, 134.0, 131.3, 131.2, 131.0, 130.1, 130.0, 128.5, 128.4, 127.5, 126.8, 126.1, 125.7, 124.0, 116.3, 116.0, 54.5, 53.7, 21.5 ppm; FT-IR (KBr): $\tilde{\nu}_{max}$=3055, 1512, 1346, 1159, 813, 592, 547, 530 cm^{-1}; HRMS (ESI): *m*/*z* $[M+H]^+$ calcd for $C_{34}H_{26}FN_2O_2S$: 545.1699; found: 545.1685.

*4.2.15. 11-(4-Fluorophenyl)-7-phenyl-9-tosyl-9,10-dihydro-8H-pyrrolo[3,4-j]phenanthridine (**4l**).* Yellow powder; 315 mg (58%); R_f=0.40 (petroleum ether/EtOAc=4:1); mp 264–265 °C; ^1H NMR (300 MHz, $CDCl_3$): δ=9.08 (s, 1H; Ar–H), 8.10 (s, 1H; Ar–H), 7.69–7.51 (m, 5H; Ar–H), 7.50–7.34 (m, 6H; Ar–H), 7.33–7.20 (m, 5H; Ar–H), 4.62 (s, 2H; –CHH–), 4.50 (s, 2H; –CHH–), 2.40 ppm (s, 3H; CH_3–); ^{13}C NMR (75 MHz, $CDCl_3$): δ=164.4, 161.1, 151.5, 145.5, 143.9, 140.1, 136.4, 136.0, 134.6, 133.7, 132.6, 131.0, 130.3, 130.1, 129.9, 129.5, 129.0, 128.6, 128.4, 127.5, 126.6, 126.1, 117.4, 117.1, 54.5, 53.8, 21.5 ppm; FT-IR (KBr): $\tilde{\nu}_{max}$=3061, 1595, 1508, 1346, 1157, 769, 590, 548, 530 cm^{-1}; HRMS (ESI): *m*/*z* $[M+H]^+$ calcd for $C_{34}H_{26}FN_2O_2S$: 545.1699; found: 545.1678.

*4.2.16. 7-(4-Fluorophenyl)-11-(o-tolyl)-9-tosyl-9,10-dihydro-8H-pyrrolo[3,4-j]phenanthridine (**3m**).* Yellow powder; 396 mg (71%); R_f=0.45 (petroleum ether/EtOAc=4:1); mp 234–235 °C; ^1H NMR (300 MHz, $CDCl_3$): δ=9.07 (s, 1H; Ar–H), 8.10 (d, *J*=7.8 Hz, 1H; Ar–H), 7.68 (d, *J*=7.7 Hz, 2H; Ar–H), 7.59–7.47 (m, 6H; Ar–H), 7.46–7.30 (m, 5H; Ar–H), 7.17 (t, *J*=7.9 Hz, 2H; Ar–H), 4.69–4.30 (m, 4H; –CHH–), 2.40 (s, 3H; CH_3–), 1.91 (s, 3H; CH_3–); ^{13}C NMR (75 MHz, $CDCl_3$): δ=164.4, 161.1, 151.4, 143.9, 139.7, 139.6, 135.2, 134.9, 134.8, 133.6, 133.5, 131.4, 131.3, 130.2, 129.9, 128.9, 128.5, 127.9, 127.7, 127.5, 126.8, 125.4, 116.3, 116.0, 54.5, 53.7, 21.5,

19.6 ppm; FT-IR (KBr): $\tilde{\nu}_{max}$=3064, 1510, 1348, 1095, 815, 742, 665, 549 cm^{-1}; HRMS (ESI): *m/z* $[M+H]^+$ calcd for $C_{35}H_{28}FN_2O_2S$: 559.1856; found: 559.1834.

*4.2.17. 11-(4-Fluorophenyl)-7-(4-methoxyphenyl)-9-tosyl-9,10-dihydro-8H-pyrrolo[3,4-j]phenanthridine (**3n**).* Yellow powder; 356 mg (62%); R_f=0.42 (petroleum ether/EtOAc=4:1); mp 236–237 °C; ^1H NMR (300 MHz, $CDCl_3$): δ=9.13 (s, 1H; Ar–H), 8.09 (d, *J*=7.9 Hz, 1H; Ar–H), 7.69 (d, *J*=7.7 Hz, 2H; Ar–H), 7.58 (t, *J*=7.3 Hz, 1H; Ar–H), 7.48 (d, *J*=8.5 Hz, 1H; Ar–H), 7.29 (s, 8H; Ar–H), 7.20–7.08 (m, 3H; Ar–H), 4.63 (s, 2H; –CHH–), 4.49 (s, 2H; –CHH–), 3.95 (s, 3H; CH_3O–), 2.40 (s, 3H; CH_3–); ^{13}C NMR (75 MHz, $CDCl_3$): δ=164.3, 161.0, 159.8, 151.6, 145.4, 143.9, 140.1, 136.4, 136.3, 136.2, 134.8, 132.3, 131.0, 130.7, 130.2, 130.1, 130.0, 129.9, 128.3, 127.9, 127.6, 126.6, 126.0, 125.9, 123.9, 117.4, 117.1, 114.5, 55.5, 54.5, 53.8, 21.5 ppm; FT-IR (KBr): $\tilde{\nu}_{max}$=3047, 1608, 1398, 1248, 1097, 812, 667, 588 cm^{-1}; HRMS (ESI): *m/z* $[M+H]^+$ calcd for $C_{35}H_{28}FN_2O_3S$: 575.1805; found: 575.1786.

*4.2.18. 7-(4-Chlorophenyl)-11-(4-fluorophenyl)-9-tosyl-9,10-dihydro-8H-pyrrolo[3,4-j]phenanthridine (**3o**).* Yellow powder; 353 mg (61%); R_f=0.38 (petroleum ether/EtOAc=4:1); mp 268–269 °C; ^1H NMR (300 MHz, $CDCl_3$): δ=9.04 (s, 1H; Ar–H), 8.11 (s, 1H; Ar–H), 7.69 (d, *J*=7.5 Hz, 2H; Ar–H), 7.57 (d, *J*=7.2 Hz, 2H; Ar–H), 7.49–7.37 (m, 6H; Ar–H), 7.36–7.19 (m, 5H; Ar–H), 4.59 (s, 2H; –CHH–), 4.48 (s, 2H; –CHH–), 2.41 ppm (s, 3H; CH_3–); ^{13}C NMR (75 MHz, $CDCl_3$): δ=164.4, 161.1, 151.3, 143.9, 140.5, 139.8, 136.2, 135.1, 134.9, 134.4, 133.6, 130.8, 130.0, 129.9, 128.5, 127.5, 126.3, 117.5, 117.1, 54.4, 53.6, 21.5 ppm; FT-IR (KBr): $\tilde{\nu}_{max}$=3064, 1597, 1508, 1346, 1014, 813, 667, 549 cm^{-1}; HRMS (ESI): *m/z* $[M+H]^+$ calcd for $C_{34}H_{25}ClFN_2O_2S$: 579.1310; found: 579.1286.

*4.2.19. 7,11-Diphenyl-9-(phenylsulfonyl)-9,10-dihydro-8H-pyrrolo[3,4-j]phenanthridine (**5p**).* Yellow powder; 379 mg (74%); R_f=0.42 (petroleum ether/EtOAc=4:1); mp 265–266 °C; ^1H NMR (300 MHz, $CDCl_3$): δ=9.07 (s, 1H; Ar–H), 8.07 (d, *J*=7.8 Hz, 1H; Ar–H), 7.78 (d, *J*=7.2 Hz, 2H; Ar–H), 7.58–7.52 (m, 5H; Ar–H), 7.51–7.45 (m, 6H; Ar–H), 7.36–7.26 (m, 4H; Ar–H), 7.13 (t, *J*=7.4 Hz, 1H; Ar–H), 4.63 (s, 2H; –CHH–), 4.52 ppm (s, 2H; –CHH–); ^{13}C NMR (75 MHz, $CDCl_3$): δ=151.6, 145.4, 140.5, 139.7, 136.5, 136.0, 133.7, 132.9, 129.5, 129.3, 129.0, 128.6, 128.5, 128.2, 127.5, 126.8, 126.0, 54.6, 53.8 ppm; FT-IR (KBr): $\tilde{\nu}_{max}$=2310, 1445, 1348, 1168, 1099, 763, 619, 594, 573 cm^{-1}; HRMS (ESI): *m/z* $[M+H]^+$ calcd for $C_{33}H_{25}N_2O_2S$: 513.1637; found: 513.1622.

*4.2.20. 7,11-Bis(4-methoxyphenyl)-9-tosyl-9,10-dihydro-8H-pyrrolo[3,4-b]phenanthridine (**6d**).* White powder; 240 mg (41%); R_f=0.45 (petroleum ether/EtOAc=6:1); mp 200–201 °C; ^1H NMR (300 MHz, $CDCl_3$): δ=9.80 (s, 1H; Ar–H), 7.74 (q, *J*=8.0 Hz, 3H; Ar–H), 7.47 (t, *J*=7.5 Hz, 1H; Ar–H), 7.33–7.18 (m, 6H; Ar–H), 6.98 (d, *J*=8.1 Hz, 2H; Ar–H), 6.83 (d, *J*=8.1 Hz, 2H; Ar–H), 6.70 (d, *J*=6.5 Hz, 2H; Ar–H), 4.78 (s, 2H; –CHH–), 4.60–4.43 (m, 2H; –CHH–), 3.87 (s, 3H; CH_3O–), 3.75 (s, 3H; CH_3O–), 2.43 ppm (s, 3H; CH_3–); ^{13}C NMR (75 MHz, $CDCl_3$): δ=191.4, 159.4, 158.7, 144.3, 143.7, 137.4, 136.7, 135.7, 135.2, 134.4, 133.5, 133.2, 131.7, 131.1, 130.9, 130.4, 129.8, 129.3, 129.2, 127.7, 127.6, 127.4, 114.3, 113.9, 113.7, 55.4, 54.0, 53.8, 21.5 ppm; FT-IR (KBr): $\tilde{\nu}_{max}$=2839, 1691, 1597, 1519, 1346, 1167, 1097, 827, 673, 549 cm^{-1}; HRMS (ESI): *m/z* $[M+H]^+$ calcd for $C_{36}H_{31}N_2O_4S$: 587.2005; found: 587.1999.

*4.2.21. 4,9-Bis(4-chlorophenyl)-2-tosyl-2,3-dihydro-1H-pyrrolo[3,4-g]isoquinoline (**7b**).* Yellow powder; 272 mg (50%); R_f=0.45 (petroleum ether/EtOAc=3:1); mp 202–203 °C; ^1H NMR (300 MHz, $CDCl_3$): δ=8.51 (s, 1H; Ar–H), 7.50 (d, *J*=7.5 Hz, 1H; Ar–H), 7.42–7.27 (m, 8H; Ar–H), 7.20 (d, *J*=7.7 Hz, 2H; Ar–H), 7.10 (d, *J*=7.6 Hz, 2H; Ar–H), 6.62 (s, 1H; Ar–H), 4.48 (s, 4H; –CHH–), 2.37 ppm (s, 3H; CH_3–); ^{13}C NMR (75 MHz, $CDCl_3$): δ=154.9, 148.7, 143.2, 137.5, 137.3, 137.0, 135.8, 135.3, 134.6, 134.0, 133.8, 133.6, 132.8, 132.6, 130.7, 130.4, 129.5, 128.7, 128.6, 127.6, 127.0, 122.7, 49.7, 47.1, 21.5 ppm; FT-IR (KBr): $\tilde{\nu}_{max}$=3030, 1489, 1334, 1157, 1095, 767, 673, 530, 509 cm^{-1}; HRMS (ESI): *m/z* $[M+H]^+$ calcd for $C_{30}H_{23}Cl_2N_2O_2S$: 545.0858; found: 545.0850.

*4.2.22. 4,9-Bis(4-fluorophenyl)-2-tosyl-2,3-dihydro-1H-pyrrolo[3,4-g]isoquinoline (**7d**).* Yellow powder; 256 mg (50%); R_f=0.36 (petroleum ether/EtOAc=3:1); mp 189–190 °C; ^1H NMR (300 MHz, $CDCl_3$): δ=8.50 (s, 1H; Ar–H), 7.49 (d, *J*=7.1 Hz, 1H; Ar–H), 7.42–7.26 (m, 8H; Ar–H), 7.16–7.07 (m, 4H; Ar–H), 6.63 (s, 1H; Ar–H), 4.48 (s, 4H; –CHH–), 2.36 ppm (s, 3H; CH_3–); ^{13}C NMR (75 MHz, $CDCl_3$): δ=163.8, 163.7, 160.5, 160.4, 155.0, 148.6, 143.1, 137.0, 136.8, 136.6, 132.8, 132.6, 131.7, 131.6, 131.2, 131.1, 130.9, 130.8, 129.9, 129.5, 127.6, 126.9, 122.5, 115.6, 115.5, 115.4, 115.3, 49.7, 47.1, 21.5 ppm; FT-IR (KBr): $\tilde{\nu}_{max}$=3034, 1599, 1506, 1338, 1157, 1093, 935, 661, 547, 526 cm^{-1}; HRMS (ESI): *m/z* $[M+H]^+$ calcd for $C_{30}H_{23}F_2N_2O_2S$: 513.1449; found: 513.1427.

*4.2.23. 6-Chloro-4-(4-chlorophenyl)-2-tosyl-2,3-dihydro-1H-benzo[f]isoindole (**9b**).* Yellow powder; 47 mg (10%); R_f=0.49 (petroleum ether/EtOAc=3:1); mp 197–198 °C; ^1H NMR (300 MHz, $CDCl_3$): δ=7.75 (d, *J*=7.5 Hz, 2H; Ar–H), 7.63–7.47 (m, 4H; Ar–H), 7.42–7.34 (m, 3H; Ar–H), 7.32 (d, *J*=7.8 Hz, 2H; Ar–H), 7.19 (d, *J*=7.8 Hz, 2H; Ar–H), 4.78 (s, 2H; –CHH–), 4.44 (s, 2H; –CHH–), 2.40 ppm (s, 3H; CH_3–); ^{13}C NMR (75 MHz, $CDCl_3$): δ=143.9, 138.1, 135.2, 134.8, 134.7, 134.4, 132.4, 131.7, 130.7, 130.5, 130.0, 129.9, 129.6, 129.5, 129.3128.9, 127.6, 127.5, 127.1, 124.3, 120.9, 118.7, 53.3, 52.9, 21.5 ppm; FT-IR (KBr): $\tilde{\nu}_{max}$=2860, 1599, 1492, 1344, 1159, 1095, 667, 605, 551 cm^{-1}; HRMS (ESI): *m/z* $[M+H]^+$ calcd for $C_{25}H_{20}Cl_2NO_2S$: 468.0593; found: 468.0586.

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Supplementary data

CCDC 809656 (**3e**) and CCDC 809657 (**8e**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif. Copies of ^1H NMR, ^{13}C NMR spectra of all compounds are provided. Supplementary data related to this article can be found online at doi:10.1016/j.tet.2011.10.041. These data include MOL files and InChiKeys of the most important compounds described in this article.

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15. Crystal structure determination: $C_{35}H_{25}Cl_3F_2N_2O_2S$ **3e**, M=681.98, triclinic, space group $P\bar{1}$, a=11.301(5), b=11.524(5), c=12.526(5) Å, U=1567.9(11) Å^3, T=293 K, Z=2, 5555 reflections measured, 13,622 unique (R_{int}=0.022), which were used in all calculations. The final $wR(F^2)$ was 0.1238 (all data). Crystal structure determination: $C_{30}H_{26}F_2N_2O_2S$ **8e**, M=2519.0(3), triclinic, space group $P\bar{1}$, a=12.6080(2), b=18.4828(12), c=12.3061(8) Å, U=2519.0(3) Å^3, T=293 K, Z=4, 5787 reflections measured, 21,530 unique (R_{int}=0.025), which were used in all calculations. The final $wR(F^2)$ was 0.0762 (all data).
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