A new entry to phenanthridine ring systems *via* sequential application of Suzuki and the modified Pictet–Spengler reactions†

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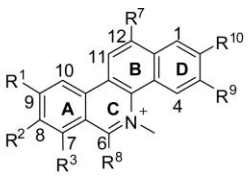
A mild, efficient and versatile method has been developed for the two step synthesis of phenanthridine ring systems using the Suzuki and the modified Pictet–Spengler strategy. The strategy involves synthesis of a substrate in which an aryl amine is tethered to an activated arene ring at the carbon ortho to the activated carbon nucleophile so as to facilitate the formation of phenanthridine ring *via* π-cyclization.

Introduction

The phenanthridine is a common pharmacophore present in a wide variety of naturally occurring phenanthridine and benzophenanthridine alkaloids. Among them nitidine (Fig. 1) and other benzo[c]phenanthridine alkaloid analogues[1] exhibit potent anti-tumor activity by the inhibition of DNA topoisomerase I,[2] and are considered as potential anti-tumor drugs.[3] However, due to their isolation in poor yields and association with broad range of anti-infectious activities,[4] search for more efficient, versatile and straightforward synthesis methods for phenanthridine ring systems with diverse physical and chemical properties has remained target of continuous investigation.[5] While traditional protocols relied extensively on Bischler–Napieralski cyclization methods,[6] strategies involving metal catalyzed reaction has been also described. Hulme and co-workers[7] applied Pd-catalyzed intramolecular Heck cyclization for the robust synthesis of phenanthridines. Similarly, nickel or palladium catalyzed iminoannulation of an internal alkyne has been used as a method to synthesize benzo[c]phenanthridines.[8] Other methods for the synthesis of phenanthridines and benzophenanthridines include either intramolecular ortho-arylation of aryl amide ions with aryl halides *via* SRN1 reactions[9] or Stille coupling of nitroarylstannanes with *o*-bromobenzaldehyde.[10] Shabashov and Daugulis reported trifluoroacetic anhydride promoted formation of phenanthridines from ortho-arylated anilides.[11] A one-pot reaction involving aromatic aldehydes, anilines and benzenediazonium-2-carboxylate has been reported for the synthesis of 6-aryl-phenanthridines *via* a cascade process.[12] However, the above reported strategies remain associated with certain disadvantages such as stringent and harsh reaction conditions, use of metal catalysts or poor generality/limited diversity.



	R^1	R^2	R^3	R^7	R^8	R^9 R^{10}
Nitidine	OMe	OMe	H	H	H	-OCH_2O-
NK109	H	OMe	OH	H	H	-OCH_2O-
7-Methoxynitidine	OMe	OMe	OMe	H	H	-OCH_2O-
7-Hydroxynitidine	OMe	OMe	OH	H	H	-OCH_2O-
9-DemethylNitidine	OH	OMe	H	H	H	-OCH_2O-
Fagaronine	OMe	OMe	H	H	H	OMe OH

Fig. 1 Structures of benzo[c]phenanthridine alkaloids.

In view of our interest in pursuing SAR studies pertaining to their anti-tumor activities, we applied the recently introduced modified Pictet–Spengler strategy[13] reported by us with the possibility of synthesizing a diverse library based upon the phenanthridine-pharmacophore. The approach involves condensation of activated heterocycle-linked aryl amine substrates with aldehydes/ketones to furnish polycyclic structures *via* π (6-endo)-cyclization. Interestingly, our approach based on an activated heterocycle holds significance towards the synthesis of phenanthridine rings since all the phenanthridine-based biologically active alkaloids in general have activating group(s) as substitution in the ring A (Fig. 2). In this report we describe a new entry to the

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† Electronic supplementary information (ESI) available: Compound characterization data of **2b**, **2e**, **2g**, **6l-w**, **7d–f**, **8h-p** and copies of ^{1}H NMR and ^{13}C NMR spectra of compounds **6a–w**, **7a–f**, and **8a–p**. See DOI: 10.1039/b905696c

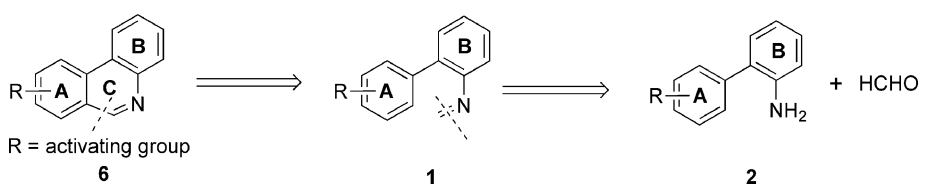


Fig. 2 Retrosynthetic analysis of phenanthridines based on the modified Pictet–Spengler strategy.

efficient synthesis of complex building block phenanthridines from commercially available starting materials.

Retrosynthetic analysis (Fig. 2) based on the modified Pictet–Spengler strategy suggests that phenanthridines could be obtained by condensing carbonyl compounds with the activated arene-linked aryl amine substrates *via* 6-endo *trig* cyclization. The most interesting feature of the strategy is the introduction of diversity at *C-6* of the phenanthridine ring since reports dealing with the synthesis of 6-substituted-phenanthridines are scarce.[12,14]

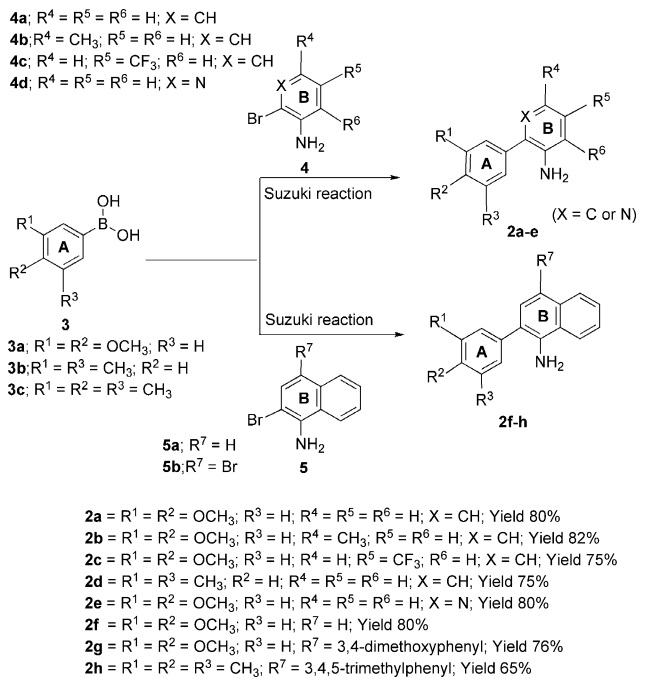
Result and discussion

The key step in our synthesis strategy involves synthesis of a substrate **2a** (Scheme 1) in which an aryl amine (ring B) is tethered to an activated arene ring A at the carbon ortho to the activated carbon nucleophile so as to facilitate the formation of a phenanthridine ring *via* a ring closure involving π-cyclization (Scheme 1). The synthesis of **2a** was affected in one step by condensing 3,4-dimethoxyphenylboronic acid **3a** with 2-bromo aniline **4a** *via* Suzuki reaction without protecting the amino functionality in 82% isolated yield. Surprisingly, reports on Pd-catalyzed Suzuki reactions involving free aryl amines are scarce.[15] We then successfully applied this strategy to the synthesis of seven additional substrates **2b-h** using three phenyl boronic acids **3a-c** and six 2-halo-arylamines **4a-d** and **5a-b** with isolated yields of substrates ranging from 65–82%. Synthesis of substrates **2a**, **2b**, **2c** **2e**, **2f** and **2g** were carried out from commercially available 3,4-dimethoxyphenylboronic acid **3a** whereas for the synthesis of substrates **2d** and **2h**, the required boronic derivatives 2-(3,5-dimethyl-phenyl)-4,4,5,5-tetramethyl-[1,3,2]dioxaborolane **3b** and 4,4,5,5-tetramethyl-2-(3,4,5-trimethyl-phenyl)-[1,3,2]dioxaborolane **3c** were obtained from their corresponding phenolic derivatives using the published procedure.[16] Similarly, while the 2-halo aryl amines derivatives **4a-d** used for Suzuki couplings were obtained from commercial sources, **5a-b** were synthesized from 1-amino naphthalene using the published procedures.[17] For the Pictet–Spengler cyclization (Scheme 2), the substrate **2a** was initially treated with 4-chlorobenzaldehyde under the traditional Pictet–Spengler protocols involving 2% TFA in DCM at both 0 °C and at room temperature. However, these resulted in the isolation of the cyclized product in >20% yield. This led us to carry out cyclization under other acidic conditions involving 1% *p*-TsOH in acetonitrile, 1% TFA in toluene, 2% TFA in toluene and 2% TFA in acetonitrile. The presence of 2% TFA in toluene effected complete conversion of **2a** and afforded **6a** in >85% purity based on HPLC (Table 1). The crude product obtained after workup was purified by silica gel column chromatography using EtOAc/hexane as an eluent and was isolated in 65% yield. The low recovery of the compound from column chromatography can be attributed to the basic nature of the compound which was evident from the fact that after reeluting the column with neat EtOAc, the remaining material was recovered albiet in >90% purity. Changing column chromatography packings from silica gel to alumina did not improve the isolated yields. The phenanthridine derivative **6a** was characterized using NMR and ESMS. As reported earlier by us,[13a,c,e,g] the π-cyclization of the imine **1** occurred *via* the formation of a dihydro derivative in the first instance, followed by spontaneous air oxidation. The strategy was then extended to the formation of benzophenanthridine rings by condensing substrate **2f** with 4-chlorobenzaldehyde in 2% TFA in toluene under reflux. As expected the reaction led to the formation of benzophenanthridine **8a** *via* π-cyclization. Next, we examined the scope and limitation of the strategy by extending the strategy to six additional variously substituted aryl amine substrates: **2b,**

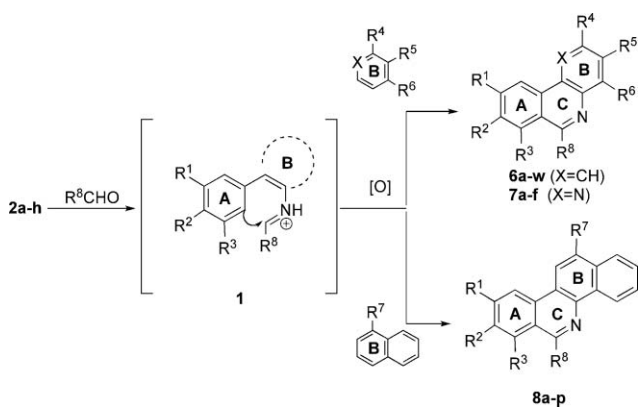
Table 1 Optimization of the reaction conditions for conversion of substrate **2a** to **6a**

Entry	Reaction Conditions	Temp/°C	Time	Yield of **6a**[a]
1.	2% TFA in DCM	rt	12 h	29
2.	1% *p*-TsOH in ACN	Reflux	12 h	30
3.	1% TFA in toluene	Reflux	12 h	35
4.	2% TFA in ACN	Reflux	12 h	30
5.	2% TFA in toluene	Reflux	12 h	65

[a] Isolated yield.



Scheme 1 General strategies for the synthesis of substrates **2a-h**.



Scheme 2 A general strategy for the modified Pictet–Spengler reaction.

Table 2 Endo cyclized products phenanthridines resulting from the condensation of substrates **2a-h** and R^8CHO

Entry	Substrate	R^8	Product	Yield (%)	t_R/min[a]
1.	**2a**	4-Cl-C_6H_4	**6a**	65	20.70
2.	**2a**	4-NO_2-C_6H_4	**6b**	60	20.32
3.	**2a**	4-Br-C_6H_4	**6c**	58	20.32
4.	**2a**	4-F-C_6H_4	**6d**	48	18.80
5.	**2a**	4-OH-C_6H_4	**6e**	45	17.27
6.	**2a**	3,4-di-(OCH_3)-C_6H_3	**6f**	50	18.65
7.	**2a**	H	**6g**	52	20.15
8.	**2b**	4-F-C_6H_4	**6h**	59	22.77
9.	**2b**	4-CN-C_6H_4	**6i**	55	20.20
10.	**2b**	3,4-di-Cl-C_6H_4	**6j**	58	24.94
11.	**2b**	3,4-di-(OCH_3)-C_6H_3	**6k**	60	22.43
12.	**2b**	C_6H_5	**6l**	54	22.80
13.	**2b**	4-Me-C_6H_4	**6m**	49	22.40
14.	**2c**	4-Cl-C_6H_4	**6n**	66	25.09
15.	**2c**	4-OEt-C_6H_4	**6o**	60	24.83
16.	**2c**	3,4-di-(OCH_3)-C_6H_3	**6p**	59	21.91
17.	**2c**	4-F-C_6H_4	**6q**	61	23.78
18.	**2c**	4-Me-C_6H_4	**6r**	56	24.57
19.	**2c**	4-$(CH_3)_2N$-C_6H_4	**6s**	60	25.51
20.	**2d**	4-Cl-C_6H_4	**6t**	53	21.45
21.	**2d**	3,4-di-(OCH_3)-C_6H_3	**6u**	55	21.55
22.	**2d**	4-OH-C_6H_4	**6v**	54	21.16
23.	**2d**	4-NO_2-C_6H_4	**6w**	56	21.09
24.	**2e**	4-F-C_6H_4	**7a**	61	18.48
25.	**2e**	4-Br-C_6H_4	**7b**	60	22.64
26.	**2e**	4-$(CH_3)_2N$-C_6H_4	**7c**	59	20.23
27.	**2e**	4-NO_2-C_6H_4	**7d**	65	19.13
28.	**2e**	4-OEt-C_6H_4	**7e**	58	21.34
29.	**2e**	4-Me-C_6H_4	**7f**	56	23.62
30.	**2f**	4-Cl-C_6H_4	**8a**	62	22.10
31.	**2f**	4-OEt-C_6H_4	**8b**	59	21.14
32.	**2f**	4-$(CH_3)_2N$-C_6H_4	**8c**	60	20.46
33.	**2f**	4-OH-C_6H_4	**8d**	57	19.18
34.	**2f**	4-NO_2-C_6H_4	**8e**	65	21.53
35.	**2g**	H	**8f**	61	21.12
36.	**2g**	4-Cl-C_6H_4	**8g**	66	22.55
37.	**2g**	3,4-di-(OCH_3)-C_6H_3	**8h**	75	21.79
38.	**2g**	4-$(CH_3)_2N$-C_6H_4	**8i**	65	20.49
39.	**2g**	4-Br-C_6H_4	**8j**	62	22.26
40.	**2g**	4-OEt-C_6H_4	**8k**	63	20.78
41.	**2g**	4-F-C_6H_4	**8l**	64	21.34
42.	**2h**	4-Cl-C_6H_4	**8m**	61	21.46
43.	**2h**	3,4-di-(OCH_3)-C_6H_3	**8n**	63	19.48
44.	**2h**	4-NO_2-C_6H_4	**8o**	60	20.56
45.	**2h**	4-Br-C_6H_4	**8p**	59	21.23

[a] Retention time on HPLC (C18 reversed-phase column; 150 × 4.6 mm; 5 μm) with a linear gradient of 10–100% CH_3CN in water over 30 min, flow rate of 1.0 mL/min, and UV detection at 220/254 nm.

2c, 2d and **2e** analogous to **2a**, and **2g** and **2h** analogous to **2f**. In all cases the substrates efficiently underwent π-cyclization when condensed with aromatic aldehydes to furnish the title compounds in satisfactory yields (Table 2). The presence of electron-donating and withdrawing group on aromatic aldehydes had no affect on cyclization, however, aliphatic aldehydes with the exception of formaldehyde and ketones failed to undergo 6-endo cyclization. All endo cyclized products reported in Table 2 are new except for compound **6g**.[18]

Conclusion

In conclusion we have developed an efficient and versatile method for the synthesis of phenanthridine rings using commercially available reactants. Our modified Pictet–Spengler strategy allows access to a three-point diversity library based upon the 6-aryl-phenanthridine core unit by promoting the π-cyclization in a wide range of activated arene-linked aryl amine substrates.

Experimental

General

All solvents were commercially available and used without purification. All products were characterized by ^{1}HNMR, ^{13}C NMR, ESMS, HRMS, IR and HPLC. Analytical TLC was performed using 2.5 × 5 cm plated coated with a 0.25 mm thickness of silica gel 60F-254 and visualization was accomplished with UV light and iodine. Column chromatography was performed using silica gel (100–200 mesh). 1H NMR spectra (300 MHz) and (200 MHz) are reported as follows: chemical shifts in ppm downfield from TMS as internal standard (δ scale), multiplicity [bs = broad singlet,

s = singlet, d = doublet, t = triplet, q=quartet, m = multiplet, o = overlapped, integration and coupling constant (Hz)]. All ^{13}C NMR spectra (75 MHz) and (50 MHz) are determined with complete proton decoupling and reported in ppm. Analytical HPLC were performed on a reverse phase C-18 column (250 mm × 4.6 mm). Retention times on HPLC (C18 reversed-phase column; 150 × 4.6 mm; 5 μm) with a linear gradient of 10–100% CH_3CN in water over 30 min, flow rate of 1.0 mL/min, and UV detection at 220/254 nm. Mass spectra were recorded on a electron-spray mass spectrometer.

Procedure for synthesis of 2-bromo-1-naphthylamine 5a. To a solution of NBS (10.0 mmol) in DCM (80.0 mL) cooled to –78 °C was added $ZrCl_4$ (0.5 mmol), followed by 1-aminonaphthalene (10.0 mmol) under nitrogen atmosphere. The reaction was carried out for 1 h and then quenched by adding saturated $NaHCO_3$ aq solution followed by extraction with CH_2Cl_2. The extracted organic phase (CH_2Cl_2) was washed with brine and dried over Na_2SO_4. The solvent was removed under pressure to give 2-bromo-1-naphthylamine **5a**. Yield = 74%, white solid, mp 73–76 °C, R_f = 0.59 (hexane), IR (KBr) ν_{max} 3401, 3050, 1625, 1503 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): 7.79–7.77 (m, 2H, ArH), 7.40 (d, 3H, J = 8.1 Hz, ArH), 7.17 (d, 1H, J = 8.8 Hz, ArH), 4.63 (s, 2H, NH_2); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 139.5, 133.2, 129.6, 128.4, 126.0, 125.6, 123.6, 121.1, 119.0, 103.9; mass (ES^+) m/z 224.0 (M^+ + 1); Anal. Calcd for $C_{10}H_8BrN$: C, 54.08; H, 3.63; N, 6.31; Found: C, 54.05; H, 3.65; N, 6.33.

Procedure for synthesis of 2,4-dibromo-naphthalen-1-amine 5b. The mixture of 1-aminonaphthalene (7 mmol) and sulfonic-acid-functionalized silica (85 mg) in 1:3 CH_3CN:Et_2O (28 mL) was treated with NBS (7.34 mmol). The mixture was stirred at room temperature and the reaction was monitored by tlc. After the completion of the reaction in 15 min, the mixture was filtered. The filtrate was concentrated and the residue was subjected to column chromatography on silica gel using (1:99 v/v) ethylacetate/hexane to obtain pure 2,4-dibromo-naphthalen-1-amine **5b**. Yield = 70%, brown solid, mp 121–123 °C, R_f = 0.58 (1:99 v/v ethylacetate/hexane), IR (KBr) ν_{max} 3427, 1633, 1425 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 8.20–8.15 (m, 1H, ArH), 7.82–7.77 (m, 2H, ArH), 7.64–7.49 (m, 2H, ArH), 4.66 (bs, 2H, NH_2); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 139.7, 132.7, 131.5, 128.1, 127.5, 126.6, 124.5, 121.5, 111.0, 103.5; mass (ES^+) m/z 301.6 (M^+ + 1); Anal. Calcd for $C_{10}H_7Br_2N$: C, 39.91; H, 2.34; N, 4.65; Found: C, 39.96; H, 2.31; N, 4.61.

General procedure for the synthesis of substrates 2a-c and 2e-g *via* Suzuki coupling

The solution of 2-bromoaniline **4a** (1 equiv) in DMF (5 mL) was degassed with nitrogen for 15 min followed by addition of Na_2CO_3 (5 mL, 2M) under continuous flow of nitrogen. After 10 min, 3,4-dimethoxyphenyl boronic acid **3a** (1.2 equiv) and $Pd(PPh_3)_4$ (0.1 equiv) were added to the reaction mixture under a nitrogen atmosphere. The reaction mixture was stirred at 80 °C for 1 h. After completion of the reaction the solution was diluted with H_2O (15 mL), and then the product was extracted three times with EtOAc (15 mL) and washed with brine. The combined organic layer was dried over anhydrous Na_2SO_4 and the solvent was removed *in vacuo*. The crude product was purified by column chromatography on silica gel using hexane:ethyl acetate (v/v) as the eluent to afford **2a**. Yield = 0.53 g (80%), white solid, mp 114–116 °C, R_f = 0.46 (1:3 v/v ethylacetate/hexane), IR (KBr) ν_{max} 3458, 3371, 1625, 1515 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 7.18–7.10 (m, 2H, ArH), 7.03–6.92 (m, 3H, ArH), 6.85–6.74 (m, 2H, ArH), 3.68 (bs, 2H, NH_2), 3.92 (s, 3H, OCH_3), 3.89 (s, 3H, OCH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 149.1, 148.2, 143.7, 132.2, 130.5, 128.4, 127.6, 121.3, 118.7, 115.6, 112.4, 111.5, 56.05, 56.0; mass (ES^+) m/z 230.2 (M^+ + 1); Anal. Calcd for $C_{14}H_{15}NO_2$: C, 73.34; H, 6.59; N, 6.11; Found: C, 73.28; H, 6.64; N, 6.07.

3′,4′-Dimethoxy-4-(trifluoromethyl)[1,1′-biphenyl]-2-amine 2c. Yield = 0.48. g (75%), brown solid, mp 150–152 °C, R_f = 0.53 (1:6 v/v ethylacetate/hexane), IR (KBr) ν_{max} 3452, 3019, 1626, 1504 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.54–7.19 (m, 2H, ArH), 7.11–6.95 (m, 4H, ArH), 3.93 (s, 3H, OCH_3), 3.90 (s, 3H, OCH_3), 3.89 (bs, 2H, NH_2); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 149.3, 148.8, 144.1, 130.7 (d, J = 8.5 Hz), 120.2 (d, J = 14.5 Hz), 115.0, 112.3, 111.9, 119.8, 111.7, 110.5, 105.9, 100.7, 56.6, 56.1; mass (ES^+) m/z 298.2 (M^+ + 1); Anal. Calcd for $C_{15}H_{14}F_3NO_2$: C, 60.60; H, 4.75; N, 4.71; Found: C, 60.65; H, 4.70; N, 4.75.

2-(3,4-Dimethoxyphenyl)naphthalen-1-amine 2f. Yield = 1.8 g (80%), brown solid, mp 136–137 °C, R_f = 0.36 (1:50 v/v ethylacetate/hexane), IR (KBr) ν_{max} 3477, 3384, 3003, 2960, 1625, 1577 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.89–7.80 (m, 2H, ArH), 7.52–7.43 (m, 2H, ArH), 7.38–7.25 (m, 2H, ArH), 7.11–6.91 (m, 3H, ArH), 3.81 (s, 2H, NH_2), 3.94 (s, 3H, OCH_3), 3.90 (s, 3H, OCH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 148.3, 138.5, 133.7, 132.7, 128.7, 128.6, 125.8, 125.4, 122.2, 121.9, 121.2, 118.6, 112.9, 111.7, 105.9, 100.7, 56.1; mass (ES^+) m/z 280.2 (M^+ + 1); Anal. Calcd for $C_{18}H_{17}NO_2$: C, 77.40; H, 6.13; N, 5.01; Found: C, 77.45; H, 6.09; N, 5.00.

Precedure for synthesis of 2,4-bis(3,4,5-trimethylphenyl)naphthalen-1-amine 2h

A mixture of trifluoro-methanesulfonic acid 3,4,5-trimethyl-phenyl ester[19] (1.0 g, 3.7 mmol) and bis(neopentyl glycolato)diboron (1.69 g, 7.5 mmol) and potassium acetate (1.1 g, 11.2 mmol) was treated with dimethyl sulfoxide (2 mL) and degassed with nitrogen for 15 min followed by addition of bis(pinacolato)diboron (0.31 g, 0.37 mmol) under continuous flow of nitrogen. The reaction mixture was stirred at 80 °C for 1 h, followed by the addition of Cs_2CO_3 (1.5 ml, 3.7M). After 10 min, 2,4-dibromo-naphthalen-1-amine **5b** (0.4 g, 1.4 mmol) and $Pd(PPh_3)_4$ (0.43 g, 0.37 mmol) were added to the reaction mixture under nitrogen atmosphere. The reaction mixture was stirred at 80 °C for 2 h. After completion of the reaction, the solution was filtered with celite, washed with EtOAc (5 mL) and this filtrate was diluted with H_2O (15 mL), and the resulting product was extracted three times with EtOAc (20 mL). The organic layer was washed with brine and dried over anhydrous Na_2SO_4 followed by the removal of solvent *in vacuo*. The crude product was purified by column chromatography on silica gel using (1:50 v/v) ethylacetate/hexane as eluent to afford 2,4-bis(3,4,5-tri methylphenyl) naphthalen-1-amine **2h**. Yield = 0.38 g (65%), semi solid, R_f = 0.52 (1:5 v/v ethylacetate/hexane), IR (KBr) ν_{max} 3783, 3017, 2924, 1614, 1449 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.98 (dd, 1H, J_1 = 8.2 Hz, J_2 = 23.5 Hz, ArH), 7.55–7.40 (m, 2H,

ArH), 7.30–7.17 (m, 2H, ArH), 6.50 (s, 4H, ArH), 4.22 (bs, 2H, NH_2), 2.34 (s, 6H, 2 × CH_3), 2.22 (s, 12H, 4 × CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 138.1 137.6, 137.2, 137.1, 136.8, 136.3, 134.1, 133.6, 131.6, 131.3, 130.5, 129.8, 129.6, 128.8, 126.9, 125.6, 125.2 125.1, 124.1, 122.3, 121.5, 114.5, 20.7, 15.4, 15.3, 14.6; mass (ES^+) *m/z* 380.5 (M^+ + 1); Anal. Calcd for $C_{28}H_{29}N$: C, 88.61; H, 7.70; N, 3.69; Found: C, 88.63; H, 7.72; N, 3.65.

Procedure for synthesis of 3′,5′-dimethyl[1,1′-biphenyl]-2-amine 2d

This was obtained in a similar manner to that described for **2h** using trifluoro-methanesulfonic acid 3,5-dimethyl-phenyl ester and 2,4-dibromo-naphthalen-1-amine **5b**.

Yield = 0.49 g (75%), liquid, R_f = 0.40 (1:25 v/v ethylacetate/hexane), IR (Neat) ν_{max} 3420, 2920, 1608, 1492 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.13 (t, 1H, *J* = 1.8 Hz, ArH), 7.10–7.06 (m, 3H, ArH), 6.99 (d, 1H, *J* = 0.6 Hz, ArH), 6.84–6.73 (m, 2H, ArH), 3.76 (bs, 2H, NH_2), 2.36 (s, 6H, 2 × CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 143.6, 139.5, 138.5, 130.5, 128.9, 128.4, 128.1, 126.9, 122.5, 118.7, 115.6, 21.5; mass (ES^+) *m/z* 198.2 (M^+ + 1); Anal. Calcd for $C_{14}H_{15}N$: C, 85.24; H, 7.66; N, 7.10; Found: C, 85.21; H, 7.64; N, 7.15.

General procedure for the Pictet–Spengler reaction leading to the synthesis of phenanthridine derivatives 6, 7 and 8. A mixture of **2** (1 equiv) and corresponding aldehyde **R**[8] (1.2 equiv) was treated with 2% solution of trifluoroactetic acid in toluene (5 mL). The reaction mixture was refluxed overnight. After completion of reaction, the toluene was evaporated *in vacuo* and the residue was extracted with aq. $NaHCO_3$ (20 mL) and EtOAc (3 × 10 mL). The combined organic layer was dried over anhydrous Na_2SO_4 and the solvent was removed *in vacuo*. The crude product was purified on silica gel column using ethylacetate/hexane (v/v) as eluent.

6-(4-Chlorophenyl)-8,9-dimethoxyphenanthridine 6a. Yield = 0.19 g (65%), white solid, mp 178–180 °C, R_f = 0.56 (1:4 v/v ethylacetate/hexane), IR (KBr) ν_{max} 3096, 2923, 1616, 1522 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 8.50–8.45 (m, 1H, ArH), 8.22–8.17 (m, 1H, ArH), 7.98 (s, 1H, ArH), 7.74–7.64 (m, 4H, ArH), 7.57–7.52 (m, 2H, ArH), 7.37 (s, 1H, ArH), 4.16 (s, 3H, OCH_3), 3.88 (s, 3H, OCH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 158.4, 152.7, 149.6, 143.5, 138.7, 134.9, 131.1, 130.5, 129.5, 128.8, 128.2, 126.8, 123.6, 121.6, 120.3, 108.0, 102.3, 56.3, 56.1; mass (ES^+) *m/z* 350.3 (M^+ + 1); Anal. Calcd for $C_{21}H_{16}ClNO_2$: C, 72.10; H, 4.61; N, 4.00; Found: C, 72.18; H, 4.66; N, 4.03.

8,9-Dimethoxy-6-(4-nitrophenyl)phenanthridine 6b. Yield = 0.23 g (60%), yellow solid, mp 228–230 °C, R_f = 0.34 (1:3 v/v ethylacetate/hexane), IR (KBr) ν_{max} 3070, 3026, 1610, 1518, 1353 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.52–8.49 (m, 1H, ArH), 8.43 (d, 2H, *J* = 8.7 Hz, ArH), 8.21–8.18 (m, 1H, ArH), 8.01 (s, 1H, ArH), 7.95 (d, 2H, *J* = 8.8 Hz, ArH), 7.76–7.66 (m, 2H, ArH), 7.27 (s, 1H, ArH), 4.18 (s, 3H, OCH_3), 3.88 (s, 3H, OCH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 157.2, 153.0, 149.9, 148.1, 146.9, 143.5, 130.8, 129.7, 128.5, 127.3, 123.9, 123.8, 121.8, 119.9, 107.4, 102.5, 56.4, 56.1; mass (ES^+) *m/z* 360.2 (M^+ + 1); Molecular Formula: $C_{21}H_{16}N_2O_4$; MS (HR EI) *m/z* calcd for $[M]^+$ 360.111 found 360.1113.

6-(4-Bromophenyl)-8,9-dimethoxyphenanthridine 6c. Yield = 0.24 g (58%), white solid, mp 193–195 °C, R_f = 0.66 (1:4 v/v ethylacetate/hexane), IR (KBr) ν_{max} 3021, 2925, 1613, 1517 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.49–8.46 (m, 1H, ArH), 8.19 (dd, 1H, J_1 = 1.4 Hz, J_2 = 8.0 Hz, ArH), 7.98 (s, 1H, ArH), 7.73–7.62. (m, 6H, ArH), 7.37 (s, 1H, ArH), 4.16 (s, 3H, OCH_3), 3.88 (s, 3H, OCH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.4, 152.7, 149.6, 143.6, 139.2, 131.8, 131.3, 130.4, 129.4, 128.2, 126.8, 123.6, 123.1, 121.6, 120.2, 107.9; 102.3, 56.3, 56.1; mass (ES^+) *m/z* 394.3 (M^+ + 1); Anal. Calcd for $C_{21}H_{16}BrNO_2$:C, 63.97; H, 4.09; N, 3.55; Found: C, 63.93; H, 4.16; N, 3.58.

6-(4-Fluorophenyl)-8,9-dimethoxyphenanthridine 6d. Yield = 0.17 g (48%), white solid, mp 188–189 °C, R_f = 0.50 (1:4 v/v ethylacetate/hexane), IR (KBr) ν_{max} 3069, 2995, 1602, 1503 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 8.49 (d, 1H, *J* = 7.38 Hz, ArH), 8.22 (d, 1H, *J* = 7.8 Hz, ArH), 7.98 (s, 1H, ArH), 7.77–7.64. (m, 4H, ArH), 7.38 (s, 1H, ArH), 7.29–7.23 (t, 2H, *J* = 9.57 Hz, ArH), 4.17 (s, 3H, OCH_3), 3.88 (s, 3H, OCH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 163.1 (d, *J* = 246.0 Hz), 158.6, 152.7, 149.5, 143.6, 136.7, 136.6, 131.5, 130.4, 129.5, 128.2, 126.7, 123.6, 121.6, 120.5, 115.6 (d, *J* = 21.5 Hz), 108.2, 102.3, 56.3, 56.0; mass (ES^+) *m/z* 334.3 (M^+ + 1); Anal. Calcd for $C_{21}H_{16}FNO_2$: C, 75.66; H, 4.84; N, 4.20; Found: C, 75.69; H, 4.88; N, 4.16.

4-(8,9-Dimethoxyphenanthridin-6-yl)phenol 6e. Yield = 0.16 g (45%), white solid, mp 248–250 °C, R_f = 0.20 (1:3 v/v ethylacetate/hexane), IR (KBr) ν_{max} 3442, 1614, 1516 cm^{-1}; ^{1}H NMR (200 MHz, DMSO-d_6): δ = 9.79 (s, 1H, OH), 8.80–8.76 (m, 1H, ArH), 8.23 (s, 1H, ArH), 8.01 (dd, 1H, J_1 = 1.7 Hz, J_2 = 7.7 Hz ArH), 7.71–7.60 (m, 4H, ArH), 7.50 (s, 1H, ArH), 6.96 (d, 2H, *J* = 12.8, ArH), 4.09 (s, 3H, OCH_3), 3.80 (s, 3H, OCH_3); ^{13}C NMR (50 MHz, DMSO-d_6): δ = 159.1, 158.5, 152.9, 149.6, 143.4, 131.6, 130.8, 129.7, 129.3, 128.4, 126.6, 123.4, 123.1, 120.0, 115.6, 108.5, 103.6, 56.6, 55.8; mass (ES^+) *m/z* 332.3 (M^+ + 1); Anal. Calcd for $C_{21}H_{17}NO_3$: C, 76.12; H, 5.17; N, 4.23; Found: C, 76.15; H, 5.21; N, 4.28.

6-(3,4-Dimethoxyphenyl)-8,9-dimethoxyphenanthridine 6f. Yield = 0.20 g (50%), white solid, mp 173–175 °C, R_f = 0.25 (2:3 v/v ethylacetate/hexane), IR (KBr) ν_{max} 3083, 3000, 2883, 1518 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 8.49–8.45 (m, 1H, ArH), 8.24–8.19 (m, 1H, ArH), 7.93 (s, 1H, ArH), 7.74–7.59. (m, 2H, ArH), 7.50 (s, 1H, ArH), 7.36–7.32 (m, 2H, ArH), 7.05 (d, 1H, *J* = 2.6 Hz, ArH), 4.16 (s, 3H, OCH_3), 3.99 (s, 3H, OCH_3), 3.96 (s, 3H, OCH_3), 3.92 (s, 3H, OCH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 159.3, 152.6, 149.7, 149.4, 149.2, 143.6, 132.9, 129.5, 128.0, 126.5, 123.5, 122.4, 121.6, 120.6, 113.0, 111.2, 108.6, 102.3, 56.2, 56.0; mass (ES^+) *m/z* 376.3 (M^+ + 1); Anal. Calcd for $C_{23}H_{21}NO_4$: C, 73.58; H, 5.64; N, 3.73; Found: C, 73.54; H, 5.69; N, 3.77.

8,9-Dimethoxy phenanthridine 6g. Yield = 0.13 g (52%), light orange solid, mp 164–165 °C [Lit[18b] 163–164 °C]; R_f = 0.32 (1:4 v/v ethylacetate/hexane), IR (KBr) ν_{max} 3068, 2942, 1609, 1508 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.65 (s, 1H, ArH), 8.58–8.55 (m, 1H, ArH), 8.44–8.41 (m, 1H, ArH), 7.97 (s, 1H, ArH), 7.87–7.85 (m, 2H, ArH), 7.55 (s, 1H, ArH), 4.25 (s, 3H, OCH_3), 4.01 (s, 3H, OCH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 158.9, 152.1, 133.0, 132.6, 131.3, 129.9, 124.2, 122.9, 122.0, 119.6, 110.2, 102.3, 57.0, 56.6; mass (ES^+) *m/z* 240.3 (M^+ + 1); Anal. Calcd for $C_{15}H_{13}NO_2$: C, 75.30; H, 5.48; N, 5.85; Found: C, 75.36; H, 5.45; N, 5.82.

6-(4-Fluorophenyl)-8,9-dimethoxy-2-methylphenanthridine 6h. Yield = 0.21 g (59%), white solid, mp 195–197 °C, R_f = 0.36 (1:4 v/v ethylacetate/hexane), IR (KBr) ν_{max} 3020, 2967, 1515, 1216 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 8.23 (s, 1H, ArH), 8.08 (d, 1H, J = 8.4 Hz ArH), 7.95 (s, 1H, ArH), 7.78–7.68. (m, 2H, ArH), 7.53 (dd, 1H, J_1 = 1.7 Hz, J_2 = 8.4 Hz, ArH), 7.36 (s, 1H, ArH), 7.29–7.20 (m, 2H, ArH), 4.18 (s, 3H, OCH_3), 3.87 (s, 3H, OCH_3), 2.65 (s, 3H, CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 163.1 (d, J = 246.0 Hz), 157.7, 152.4, 149.4, 141.9, 136.6, 136.5, 131.6, 131.4, 130.1, 130.0, 129.1, 123.4, 121.1, 120.5, 115.6 (d, J = 21.5 Hz), 108.0, 102.2, 56.3, 56.0, 22.1; mass (ES^+) m/z 348.3 (M^+ + 1); Anal. Calcd for $C_{22}H_{18}FNO_2$: C, 76.06; H, 5.22; N, 4.03; Found: C, 76.16; H, 5.25; N, 4.09.

4-(8,9-Dimethoxy-2-methylphenanthridin-6-yl)benzonitrile 6i. Yield = 0.20 g (55%), light brown, mp >250 °C, R_f = 0.38 (1:5 v/v ethylacetate/hexane), IR (KBr) ν_{max} 3003, 2912, 2226, 1519 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 8.25 (s, 1H, ArH), 8.07 (d, 1H, J = 8.3 Hz, ArH), 7.97 (s, 1H, ArH), 7.90–7.83. (m, 4H, ArH), 7.56 (dd, 1H, J_1 = 1.3 Hz, J_2 = 8.3 Hz, ArH), 7.26 (s, 1H, ArH), 4.18 (s, 3H, OCH_3), 3.87 (s, 3H, OCH_3), 2.66 (s, 3H, CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 156.5, 152.7, 149.7, 145.0, 141.8, 137.2, 132.4, 130.5, 130.2, 129.3, 123.6, 121.2, 119.9, 118.8, 112.5, 107.3, 102.4, 56.3, 56.0, 22.1; mass (ES^+) m/z 355.3 (M^+ + 1); Anal. Calcd for $C_{23}H_{18}N_2O_2$: C, 77.95; H, 5.12; N, 7.90; Found: C, 77.87; H, 5.08; N, 7.92.

6-(3,4-Dichlorophenyl)-8,9-dimethoxy-2-methyl phenanthridine 6j. Yield = 0.23 g (58%), white solid, mp 214–215 °C, R_f = 0.45 (1:5 v/v ethylacetate/hexane), IR (KBr) ν_{max} 2943, 1618, 1520 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 8.23 (s, 1H, ArH), 8.07 (d, 1H, J = 8.3 Hz, ArH), 7.95. (s, 1H, ArH), 7.88 (s, 1H, ArH), 7.64–7.52 (m, 3H, ArH), 7.32 (s, 1H, ArH), 4.17 (s, 3H, OCH_3), 3.89 (s, 3H, OCH_3), 2.65 (s, 3H, CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 156.0, 152.7, 149.6, 141.7, 140.2, 137.0, 133.0, 131.8, 130.5, 130.2, 130.0, 129.2, 129.0, 123.5, 121.1, 120.0, 107.5, 102.3, 56.3, 56.1, 22.2; mass (ES^+) m/z 398.2 (M^+ + 1); Anal. Calcd for $C_{22}H_{17}C_{l2}NO_2$: C, 66.34; H, 4.30; N, 3.52; Found: C, 66.39; H, 4.27; N, 3.49.

6-(3,4-Dimethoxyphenyl)-8,9-dimethoxy-2-methyl phenanthridine 6k. Yield = 0.26 g (60%), yellow solid, mp 211–212 °C, R_f = 0.15 (1:4 v/v ethylacetate/hexane), IR (KBr) ν_{max} 2936, 2835, 1612, 1517 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 8.22 (s, 1H, ArH), 8.09 (d, 1H, J = 8.4 Hz, ArH), 7.95 (s, 1H, ArH), 7.52 (d, 2H, J = 4.2 Hz, ArH), 7.32–7.27 (m, 1H, ArH), 7.05 (d, 2H, J = 8.7 Hz, ArH), 4.17 (s, 3H, OCH_3), 3.98 (s, 3H, OCH_3), 3.95 (s, 3H, OCH_3), 3.88 (s, 3H, OCH_3), 2.64 (s, 3H, CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 158.4, 152.3, 149.5, 149.3, 149.1, 142.0, 136.3, 132.6, 130.1, 129.9, 129.1, 122.4, 121.1, 113.0, 111.2, 108.5, 102.2, 56.3 56.2, 56.1, 56.0, 22.0; Molecular Formula: $C_{24}H_{23}NO_4$; mass: (ES^+) m/z 390.3 (M^+ + 1); MS (HR EI) m/z calcd for $[M]^+$ 389.1627 found 389.1634.

6-(4-Fluorophenyl)-8,9-dimethoxy-6a,10a-dihydrobenzo [*c*][1,5]-naphthyridine7a. Yield = 0.19 g (61%), white solid, mp 163–165 °C, R_f = 0.48 (2:3 v/v ethylacetate/hexane), IR (KBr) ν_{max} 3021, 1610, 1515 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 8.97 (dd, 1H, J_1 = 1.6 Hz, J_2 = 4.3 Hz, ArH), 8.66 (s, 1H, ArH), 8.46 (dd, 1H, J_1 = 1.6 Hz, J_2 = 8.3 Hz, ArH), 7.79–7.74 (m, 2H, ArH), 7.67–7.63 (m, 1H, ArH), 7.38 (s, 1H, ArH), 7.31–7.25 (m, 2H, ArH), 4.21 (s, 3H, OCH_3), 3.91 (s, 3H, OCH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 163.3 (d, J = 247.5 Hz), 159.4, 153.0, 150.9, 149.0, 140.5, 138.3, 137.4, 136.0, 135.9, 131.5, 131.4, 130.6, 126.8, 123.4, 122.5, 115.7 (d, J = 21.0 Hz), 107.5, 103.5, 56.6, 56.1; mass (ES^+) m/z 335.3 (M^+ + 1); Anal. Calcd for $C_{20}H_{15}FN_2O_2$: C, 71.85; H, 4.52; N, 8.38; Found: C, 71.81; H, 4.56; N, 8.35.

6-(4-Bromophenyl)-8,9-dimethoxy-6a,10a-dihydrobenzo[*c*][1,5]-naphthyridine7b. Yield = 0.20 g (60%), brown solid, mp 187–189 °C, R_f = 0.42 (1:4 v/v ethylacetate/hexane), IR (KBr) ν_{max} 3020, 1597, 1521 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 8.98 (dd, 1H, J_1 = 1.6 Hz, J_2 = 4.3 Hz, ArH), 8.65 (s, 1H, ArH), 8.45 (dd, 1H, J_1 = 1.6 Hz, J_2 = 8.3 Hz, ArH), 7.74–7.63 (m, 5H, ArH), 7.37 (s, 1H, ArH), 4.22 (s, 3H, OCH_3), 3.92 (s, 3H, OCH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 159.2, 153.1, 150.9, 149.2, 140.5, 138.8, 138.3, 137.5, 131.9, 131.3, 130.9, 130.6, 131.4, 123.4, 122.3, 107.3, 103.5, 56.6, 56.2; mass (ES^+) m/z 395.3 (M^+ + 1); Anal. Calcd for $C_{20}H_{15}BrN_2O_2$: C, 60.78; H, 3.83; N, 7.09; Found: C, 60.72; H, 3.87; N, 7.04.

4-(8,9-Dimethoxy-6a,10a-dihydrobenzo[*c*][1,5] naphthyridin-6-yl)-*N*,*N*-dimethylaniline 7c. Yield = 0.18 g (59%), yellowish green solid, mp 157–159 °C, R_f = 0.26 (1:1 v/v ethylacetate/hexane), IR (KBr) ν_{max} 2930, 1610, 1516 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 8.92 (dd, 1H, J_1 = 1.6 Hz, J_2 = 4.3 Hz, ArH), 8.62 (s, 1H, ArH), 8.44 (dd, 1H, J_1 = 1.7 Hz, J_2 = 8.3 Hz, ArH), 7.75–7.57. (m, 4H, ArH), 6.90 (d, 2H, J = 8.9 Hz, ArH), 4.21 (s, 3H, OCH_3), 3.95 (s, 3H, OCH_3), 3.07 (s, 6H, 2 x CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 160.7, 152.6, 151.1, 150.6, 149.5, 148.3, 145.0, 140.0, 137.2, 130.8, 130.5, 127.7, 122.8, 120.7, 112.2, 111.2, 108.3, 103.4, 56.5, 56.2, 56.1, 56.0, 40.5; mass (ES^+) m/z 360.4 (M^+ + 1); Molecular Formula: $C_{22}H_{21}N_3O_2$; MS (HR EI) m/z calcd for $[M]^+$ 359.1634 found 359.1624.

6-(4-Chlorophenyl)-8,9-dimethoxybenzo[*c*]phenanthridine 8a. Yield = 0.18 g (62%), white solid, mp 215–217 °C, R_f = 0.43 (1:15 v/v ethylacetate/hexane), IR (KBr) ν_{max} 3003, 2924, 1616, 1580 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 9.40 (d, 1H, J = 8.0 Hz, ArH), 8.42 (d, 1H, J = 9.0 Hz, ArH), 7.99–7.94. (m, 3H, ArH), 7.86 (d, 2H, J = 8.4 Hz, ArH), 7.73–7.63 (m, 2H, ArH), 7.57 (d, 2H, J = 8.4 Hz, ArH), 7.53 (s, 1H, ArH), 4.18 (s, 3H, OCH_3), 3.92 (s, 3H, OCH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 156.1, 152.5, 149.5, 140.3, 139.2, 134.8, 133.0, 132.3, 131.6, 130.0, 128.7, 127.6, 127.3, 127.2, 126.9, 124.9, 120.5, 120.1, 119.7, 107.2, 102.1, 56.2, 56.0 mass (ES^+) m/z 400.3 (M^+ + 1); Anal. Calcd for $C_{25}H_{18}ClNO_2$: C, 75.09; H, 4.54; N, 3.50; Found: C, 75.05; H, 4.59; N, 3.53.

8,9-Dimethoxy-6-(4-ethoxyphenyl)benzo[*c*]phenanthridine 8b. Yield = 0.16 g (59%), white solid, mp 162–165 °C, R_f = 0.46 (1:12 v/v ethylacetate/hexane), IR (KBr) ν_{max} 3019, 2977, 1610, 1516 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 9.46 (dd, 1H, J_1 = 1.7 Hz, J_2 = 9.4 Hz, ArH), 8.42 (d, 1H, J = 9.1 Hz, ArH), 7.98–7.85. (m, 5H, ArH), 7.74–7.60 (m, 3H, ArH), 7.12 (d, 2H, J = 8.7 Hz, ArH), 4.16 (s, 3H, OCH_3), 4.16 (q, 2H, J = 6.9 Hz, OCH_2), 3.93 (s, 3H, OCH_3), 1.50 (t, 3H, J = 7.0 Hz, CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 159.5, 157.5, 153.0, 152.4, 149.3, 133.0, 132.4, 131.6, 130.0, 127.6, 127.1, 126.9, 126.7, 125.1, 119.9, 119.8, 114.5, 109.7, 107.9, 102.1, 63.7, 56.1, 56.0, 15.0; mass (ES^+) m/z 410.3 (M^+ + 1); Anal. Calcd for $C_{27}H_{23}NO_3$: C, 79.20; H, 5.66; N, 3.42; Found: C, 79.22; H, 5.64; N, 3.43.

8,9-Dimethoxy-6-(4-*N*,*N*-dimethylaminephenyl)benzo[*c*] phenanthridine 8c. Yield = 0.16 g (60%), light yellow solid, mp 165–166 °C, R_f = 0.44 (1:15 v/v ethylacetate/hexane), IR (KBr) ν_{max} 3021, 1608, 1521 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 9.48 (dd, 1H, J_1 = 1.7 Hz, J_2 = 9.0 Hz, ArH), 8.43 (d, 1H, J = 9.1 Hz, ArH), 7.99–7.87 (m, 5H, ArH), 7.80 (s, 1H, ArH), 7.74–7.59 (m, 2H, ArH), 6.94 (d, 2H, J = 8.8 Hz, ArH), 4.18 (s, 3H, OCH_3), 3.96 (s, 3H, OCH_3), 3.09 (s, 6H, 2 x CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 157.8, 152.3, 150.9, 149.3, 140.6, 133.1, 132.5, 131.4, 130.1, 128.8, 127.5, 127.0, 126.6, 126.5, 125.2, 121.0, 119.9, 119.7, 112.2, 108.3, 102.2, 56.2, 56.1, 40.6; mass (ES^+) m/z 409.3 (M^+ + 1); Anal. Calcd for $C_{27}H_{24}N_2O_2$: C, 79.39; H, 5.92; N, 6.86; Found: C, 79.41; H, 5.87; N, 6.88.

4-(8,9-Dimethoxybenzo[*c*]phenanthridin-6-yl)phenol 8d. Yield = 0.15 g (57%), white solid, mp >250 °C, R_f = 0.39 (1:10 v/v ethylacetate/hexane), IR (KBr) ν_{max} 3435, 3020, 1609, 1518 cm^{-1}; ^1H NMR (200 MHz, DMSO-d_6): δ = 9.82 (s, 1H, OH), 9.24 (dd, 1H, J_1 = 2.7 Hz, J_2 = 6.1 Hz, ArH), 8.79 (d, 1H, J = 9.2 Hz, ArH), 8.26 (s, 1H, ArH), 8.06 (d, 2H, J = 9.1 Hz, ArH), 7.78–7.62 (m, 5H, ArH), 7.0 (d, 2H, J = 8.5 Hz, ArH), 4.11 (s, 3H, OCH_3), 3.83 (s, 3H, OCH_3); ^{13}C NMR (50 MHz, DMSO-d_6): δ = 158.0, 157.0, 152.5, 149.3, 139.3, 132.6, 131.5, 131.3, 130.9, 129.5, 127.7, 127.0, 126.6, 126.5, 124.1, 120.9, 120.0, 119.6, 115.2, 107.3, 103.0, 56.1, 55.3; mass (ES^+) m/z 382.3 (M^+ + 1); Anal. Calcd for $C_{25}H_{19}NO_3$: C, 78.72; H, 5.02; N, 3.67; Found: C, 78.69; H, 5.07; N, 3.71.

8,9-Dimethoxy-6-(4-nitrophenyl)benzo[*c*]phenanthridine 8e. Yield = 0.19 g (65%), yellow solid, mp >250 °C, R_f = 0.42 (1:10 v/v ethylacetate/hexane), IR (KBr) ν_{max} 2925, 1601, 1514, 1349 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 9.38 (d, 1H, J = 8.7 Hz, ArH), 8.47 (d, 2H, J = 8.8 Hz, ArH), 8.12–7.96 (m, 3H, ArH), 7.77–7.67 (m, 2H, ArH), 7.45 (s, 1H, ArH), 7.08–7.05 (m, 2H, ArH), 6.93 (d, 1H, J = 8.1 Hz, ArH), 3.95 (s, 3H, OCH_3), 3.92 (s, 3H, OCH_3); ^{13}C NMR (75 MHz, $CDCl_3$+TFA): δ = 159.3, 152.8, 151.7, 150.0, 136.4, 135.0, 133.8, 132.1, 131.6, 130.5, 130.4, 129.7, 126.6, 124.5, 123.6, 123.2, 121.5, 119.8, 112.9, 112.1, 110.9, 107.5, 103.0, 57.3, 56.5; mass (ES^+) m/z 411.2 (M^+ + 1); Anal. Calcd for $C_{25}H_{18}N_2O_4$: C, 73.16; H, 4.42; N, 6.83; Found: C, 73.12; H, 4.45; N, 6.79.

12-(3,4-Dimethoxyphenyl)-8,9-dimethoxy benzo[c]phenanthridine 8f. Yield = 0.13 g (61%), white solid, mp 225–227 °C, R_f = 0.41 (1:5 v/v ethylacetate/hexane), IR (KBr) ν_{max} 3021, 2978, 1617, 1514 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 9.51–9.47 (m, 1H, ArH), 9.34 (s, 1H, ArH), 8.32 (s, 1H, ArH), 7.99–7.91 (m, 2H, ArH), 7.81–7.73 (m, 1H, ArH), 7.66–7.58 (m, 1H, ArH), 7.44 (s, 1H, ArH), 7.22–7.10 (s, 3H, ArH), 4.14 (s, 3H, OCH_3), 4.11 (s, 3H, OCH_3), 4.01 (s, 3H, OCH_3) 3.94 (s, 3H, OCH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 153.2, 150.1, 149.9, 148.9, 148.8, 140.5, 139.4, 133.7, 132.5, 132.0, 128.8, 127.2, 126.9, 126.3, 124.9, 122.9, 122.5, 120.6, 120.2, 113.8, 111.3, 107.4, 101.8, 56.4, 56.2, 56.1; mass (ES^+) m/z 426.3 (M^+ + 1); Anal. Calcd for $C_{27}H_{23}NO_4$: C, 76.22; H, 5.45; N, 3.29; Found: C, 76.26; H, 5.48; N, 3.24.

6-(4-Chlorophenyl)-12-(3,4-dimethoxyphenyl)-8,9-dimethoxy benzo[c]phenanthridine 8g. Yield = 0.17 g (66%), white solid, mp 250 °C, R_f = 0.39 (1:4 v/v ethylacetate/hexane), IR (KBr) ν_{max} 3021, 1601, 1518 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 9.54–9.51 (m, 1H, ArH), 8.34 (s, 1H, ArH), 7.99–7.88 (m, 4H, ArH), 7.75–7.70 (m, 1H, ArH), 7.64–7.57 (m, 4H, ArH), 7.22–7.16 (m, 2H, ArH), 7.09 (d, 1H, J = 8.2 Hz, ArH), 4.15 (s, 3H, OCH_3), 4.02 (s, 3H, OCH_3), 3.95 (s, 3H, OCH_3), 3.94 (s, 3H, OCH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 156.2, 152.7, 149.7, 148.9, 148.8, 139.9, 139.5, 139.3, 134.8, 133.8, 132.6, 132.2, 131.6, 130.0, 128.7, 127.2, 126.8, 126.2, 125.3, 122.6, 120.9, 120.5, 119.7, 113.8, 111.3, 107.4, 102.3, 56.4, 56.3, 56.2, 56.1; Molecular Formula: $C_{33}H_{26}ClNO_4$; mass (ES^+) m/z 536.4 (M^+ + 1); MS (HR EI) m/z calcd for $[M]^+$ 536.15433 found 536.15438.

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