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ORIGINAL ARTICLE

A facile solvent-free three-component domino synthesis of novel 2,4-diaryl-5,6-dihydrobenzo[*j*][1,7]phenanthrolines

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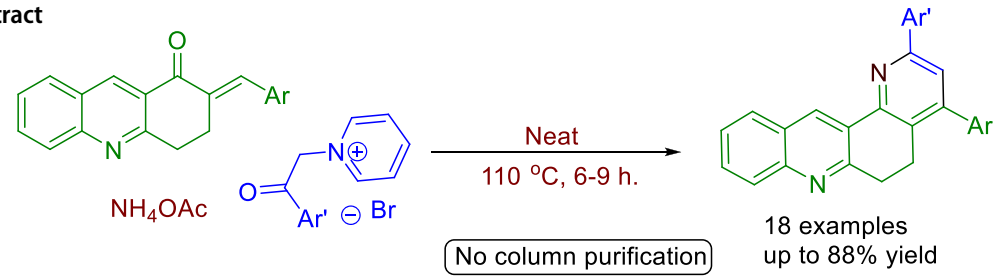
Abstract

A simple, efficient and green procedure for the synthesis of novel 2,4-diaryl-5,6-dihydrobenzo[*j*][1,7]phenanthrolines has been developed via a Krohnke-type one-pot three-component reaction of 2-[arylmethylidene]-3,4-dihydro-1(2*H*)-acridinones and (2-aryl-2-oxoethyl)pyridinium bromides in the presence of excess ammonium acetate in good yields under solvent-free conditions. Good functional group tolerance, high substrate scope and no column purification are the practical advantages of this methodology.

Graphical abstract



Keywords Multicomponent domino reaction · Solvent-free reaction · Green chemistry · Dihydrobenzo[*j*][1,7]phenanthrolines · MCRs

Introduction

In recent years, sustainable synthetic methods have gained more attention as they address many environmental problems [1, 2]. Among them, solvent-free methods [3, 4] are an attractive tool for the synthesis of biologically active frameworks. Multicomponent domino reactions are an interesting strategy due to the great synthetic efficiency in a one-pot operation [5–11]. These protocols have rendered many advantages including convergent routes, facile automation and reduction of workup stages, extraction and purification processes. Needless to say, the combination of these two protocols can be effective in the construction of novel heterocycles in the greener perspective [12].

Molecular frameworks comprising quinoline/pyridine bear potential for biological and medicinal applications [13, 14]. In particular, the phenanthroline core presents in many natural

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products such as meridine and ascididemin [15] and some synthetic phenanthrolines display significant antitumor activities [16, 17] (Fig. 1) besides serving as ligands [18, 19] and organic semiconductor materials [20]. Benzophenanthrolines also serve as protein tyrosine kinase inhibitors, which can be used in mammalian carcinomas [21].

It is interesting to note that syntheses of benzophenanthrolines are relatively scarce in the literature, and one of such syntheses is the reaction between (*E*)-2-benzylidene-7-chloro-9-phenyl-3,4-dihydroacridin-1(2*H*)-one and malononitrile in the presence of NaH in refluxing ethanol–benzene mixture or in the presence of montmorillonite KSF in ethanol [22]. This method uses toxic solvents and offers a limited substrate scope. In this context, here we disclose the assembly of novel benzophenanthrolines viz 2,4-diaryl-5,6-dihydrobenzo[*j*][1,7]phenanthrolines, (Scheme 1). The final products bear structural resemblance to quinoline-based heterocycles. The present study is the part of our ongoing research program on the assembly of novel biologically relevant heterocycles through multicomponent/domino and green transformations [23–27].

Results and discussion

The present study commenced with the optimization of a model three-component reaction between 2-[4-bromobenzylidene]-3,4-dihydro-1-(2*H*)-acridinone, 1-(2-oxo-2-

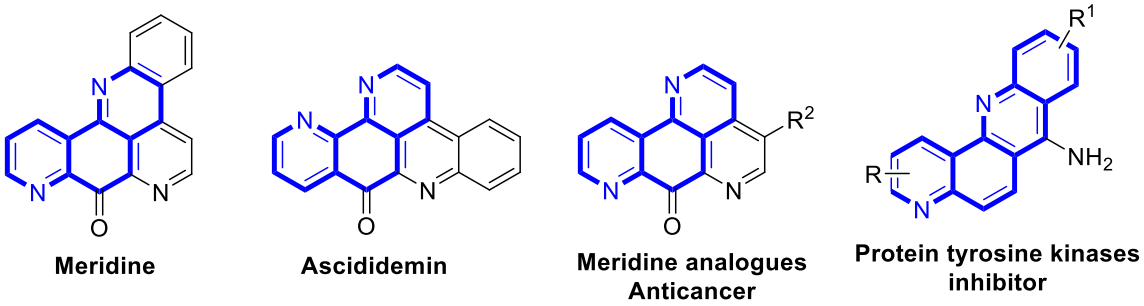
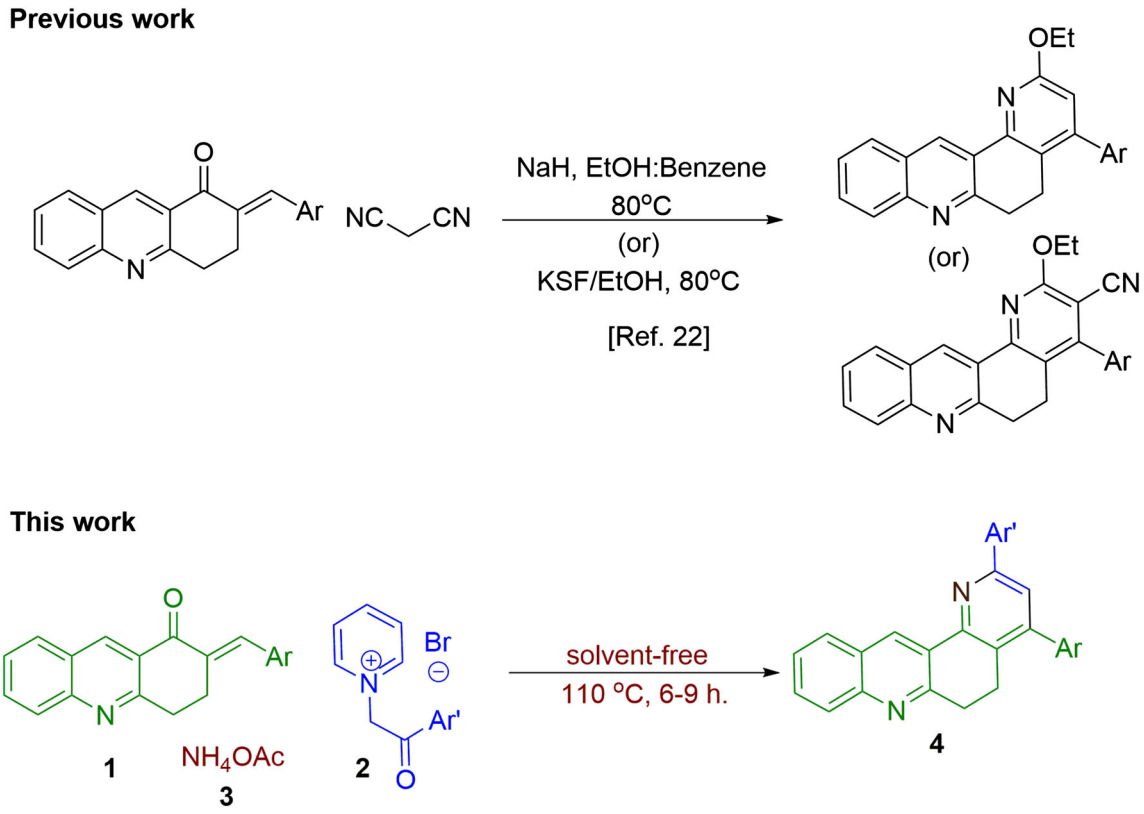
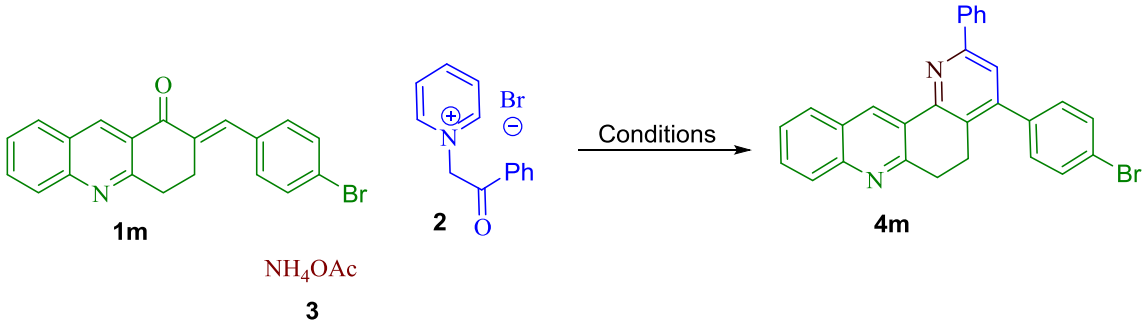


Fig. 1 Naturally occurring phenanthroline derivatives, meridine analogues and biologically active benzophenanthroline



Scheme 1 Outline of this work

Table 1 Solvent influence on the synthesis of **4m**



Entry	Solvent	Time (h)	Yield of **4m** (%)[a]	Temp. (°C)
1	Water	12	35	Reflux
2	DMF	11	58	120
3	Diethylene glycol	12	19	120
4	EtOH	8	84 (78)	Reflux
5	MeOH	8	71 (65)	Reflux
6	Neat	6	89 (81)	110
7	CH_3CN	12	39	Reflux
8	THF	11	48	Reflux

[a]Isolated yield after purification by column chromatography. Yields in brackets are after recrystallization from ethanol

phenylethyl)pyridin-1-ium bromide and ammonium acetate. This reaction was explored in different solvents, viz. methanol, ethanol, water, diethylene glycol, *N,N*-dimethylformamide, acetonitrile, tetrahydrofuran, and also under solvent-free conditions (Table 1).

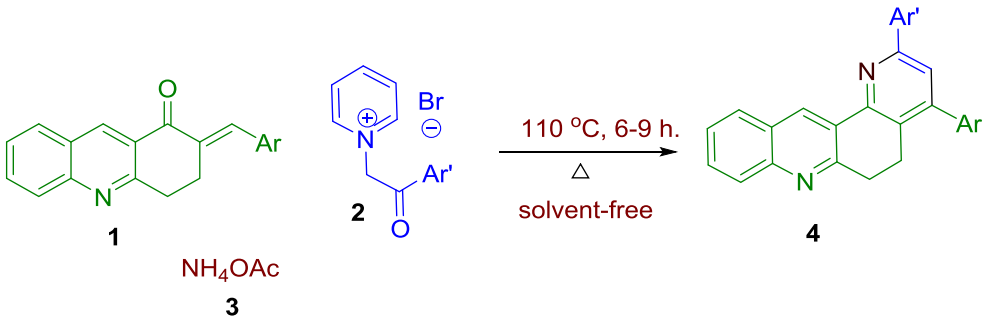
As can be seen from the data listed in Table 1, the best result was obtained by heating the reaction mixture under solvent-free conditions at 110 °C to furnish 4-(4-bromophenyl)-2-phenyl-5,6-dihydrobenzo[*j*][1,7]-phenanthroline (**4m**) in 81% yield (Table 1, entry 6). Protic solvents (ethanol, methanol) afforded higher yields than the other solvents tested.

Having established the optimal conditions for our reaction, the scope of the reaction was first examined focusing on the 2-[arylmethylidene]-3,4-dihydro-1(2*H*)-acridinone component. Acridinones bearing electron-withdrawing and electron-donating groups in the aryl part proceeded smoothly to give the respective products (Table 2). Similarly, for 1-(2-oxo-2-arylethyl)pyridin-1-ium bromides, the presence of electron-donating, neutral and electron-withdrawing groups in the aryl part is well tolerated, affording products in good yields (Table 2). A practical advantage of this protocol is the fact that no column purification is needed. After completion of the reaction (monitoring by TLC), the mixture was treated with ice water and the resulting solid **4** was filtered and washed with water. Single recrystallization of the product from ethanol afforded analytically pure samples. To the best of our knowledge, this is the first report of a multicomponent reaction employing pyridinium ylides generated in situ for the construction of 2,4-diaryl-5,6-dihydrobenzo[*j*][1,7]-phenanthrolines under solvent-free conditions.

The structures of products **4** were deduced from one- and two-dimensional NMR spectroscopic data as detailed for **4n** as a representative example (Fig. 2). In the ^{1}H NMR spectrum of **4n**, the H-3 appears as a singlet at 7.59 ppm, which shows (i) a C,H-COSY correlation with the signal at 120.0 ppm due to C-3 and (ii) HMBCs with C-2, C-1′, and C-4a, appearing at 154.1, 137.4, and 128.0 ppm, respectively. The 5-CH_2 hydrogen atoms appear as a multiplet around 3.09–3.13 ppm. These hydrogen atoms show (i) H,H-COSY correlation with 6-CH_2 hydrogen atoms, (ii) C,H-COSY correlations with C-5 at 24.7 ppm, and HMBCs with C-6 at 31.9 ppm, C-4a at 128.0 ppm, C-6a at 158.9 ppm and C-12b at 151.6 ppm. The multiplet at 3.26–3.30 ppm arises from the 6-CH_2 hydrogens which show (i) H,H-COSY correlation with 5-CH_2 hydrogens (ii) C,H-COSY correlation with C-6 at 31.9 ppm, and HMBCs with C-5, C-4a, and C-6a, appearing at 24.7, 128.0, and 158.9 ppm, respectively. The H-12 appears as a singlet at 9.23 ppm, which shows (i) C,H-COSY correlation with carbon signal at 132.7 ppm due to C-12, and HMBCs with C-11 at 128.8 ppm, C-6a at 158.9 ppm, C-7a at 148.0 ppm, and C-12b at 151.6 ppm. Finally, the structure of the compound was confirmed by single-crystal X-ray crystallography of **4g** (Fig. 3).

A plausible mechanism for the formation of 2,4-diaryl-5,6-dihydrobenzo[*j*][1,7]phenanthrolines **4** is depicted in

Table 2 Synthesis of 2,4-diaryl-5,6-dihydrobenzo[*j*][1,7]phenanthrolines **4**



Entry	Comp.	Ar	Ar′	Yield (%)[a]
1	**4a**	4-MeC_6H_4	4-MeC_6H_4	83
2	**4b**	4-MeC_6H_4	4-$MeOC_6H_4$	84
3	**4c**	4-MeC_6H_4	C_6H_5	81
4	**4d**	4-MeC_6H_4	4-FC_6H_4	86
5	**4e**	4-MeC_6H_4	4-$O_2NC_6H_4$	76
6	**4f**	2-$MeOC_6H_4$	4-$MeOC_6H_4$	77
7	**4g**	2-$MeOC_6H_4$	C_6H_5	82
8	**4 h**	2-$MeOC_6H_4$	4-FC_6H_4	78
9	**4i**	2-$MeOC_6H_4$	4-ClC_6H_4	85
10	**4j**	4-ClC_6H_4	4-FC_6H_4	86
11	**4k**	4-BrC_6H_4	4-MeC_6H_4	87
12	**4l**	4-BrC_6H_4	4-$MeOC_6H_4$	83
13	**4m**	4-BrC_6H_4	C_6H_5	81
14	**4n**	4-BrC_6H_4	4-ClC_6H_4	88
15	**4o**	3-$O_2NC_6H_4$	4-MeC_6H_4	76
16	**4p**	3-$O_2NC_6H_4$	4-FC_6H_4	80
17	**4q**	3-$O_2NC_6H_4$	4-ClC_6H_4	77
18	**4r**	3-$O_2NC_6H_4$	C_6H_5	75

[a]Isolated yield after recrystallization from ethanol

Scheme 2. The Michael addition of pyridinium ylide **5** (generated in situ from **2**) to **1** presumably affords pyridinium enolate **6**, which subsequently reacts with ammonia available from the dissociation of ammonium acetate to afford enamine **8** via **7**. Intermediate **5** is ultimately transformed into product **4** via elimination–condensation reactions. Another plausible mechanism involves the hemiaminal formation and intramolecular attack onto the other carbonyl followed by elimination.

It is interesting that the other possible product **4′** via chemoselective intramolecular S_N2 substitution [28–30] is not formed at all.

Conclusion

In summary, we have described a facile synthesis of novel dihydrobenzo[*j*][1,7]phenanthrolines through solvent-free Krohnke-type one-pot three-component domino reactions of 2-[arylmethylidene]-3,4-dihydro-1(2*H*)-acridinones and 1-(2-oxo-2-arylethyl)pyridin-1-ium bromide in the presence of excess ammonium acetate. This protocol avoids the use of expensive catalysts, toxic solvents and chromatographic separation.

Experimental part

General

All melting points reported in this work were measured in open capillaries and are uncorrected (Sigma, 71281). Silica gel-G plates (Merck) were used for TLC analysis with a mixture of petroleum ether of boiling range 60–80 °C and ethyl acetate as eluent. ^1H and ^{13}C NMR spectra were recorded at 300 and 75 MHz, respectively, on a Bruker 300 MHz (Avance) instrument using either $CDCl_3$ or DMSO-d_6 and tetramethylsilane as the internal standard.

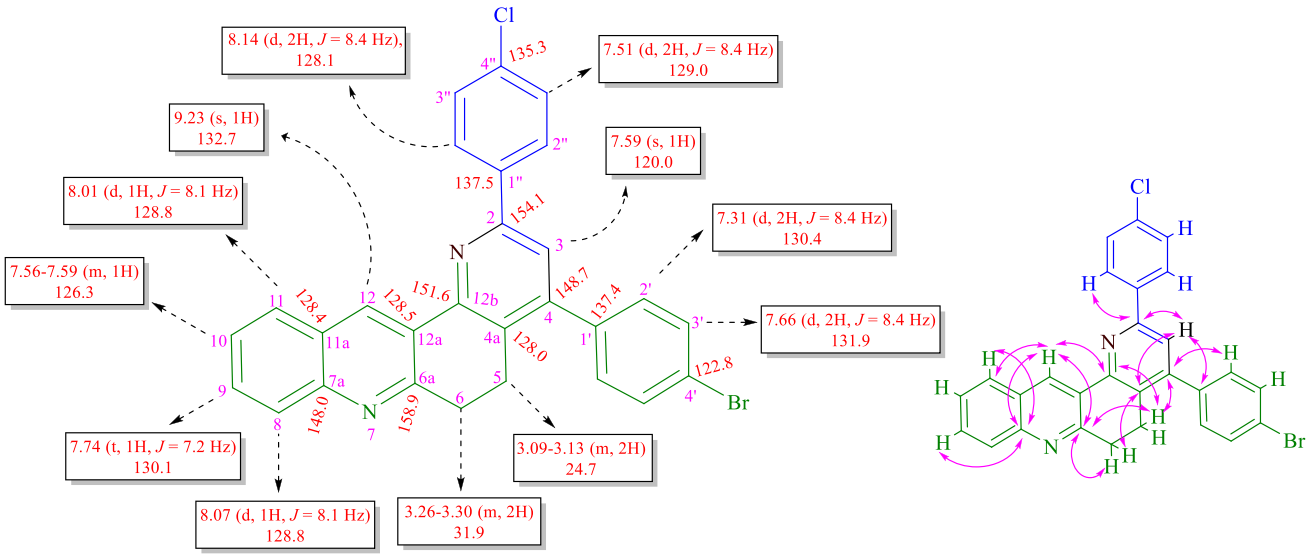


Fig. 2 ^{1}H and ^{13}C NMR chemical shifts and selected HMBCs of **4n**

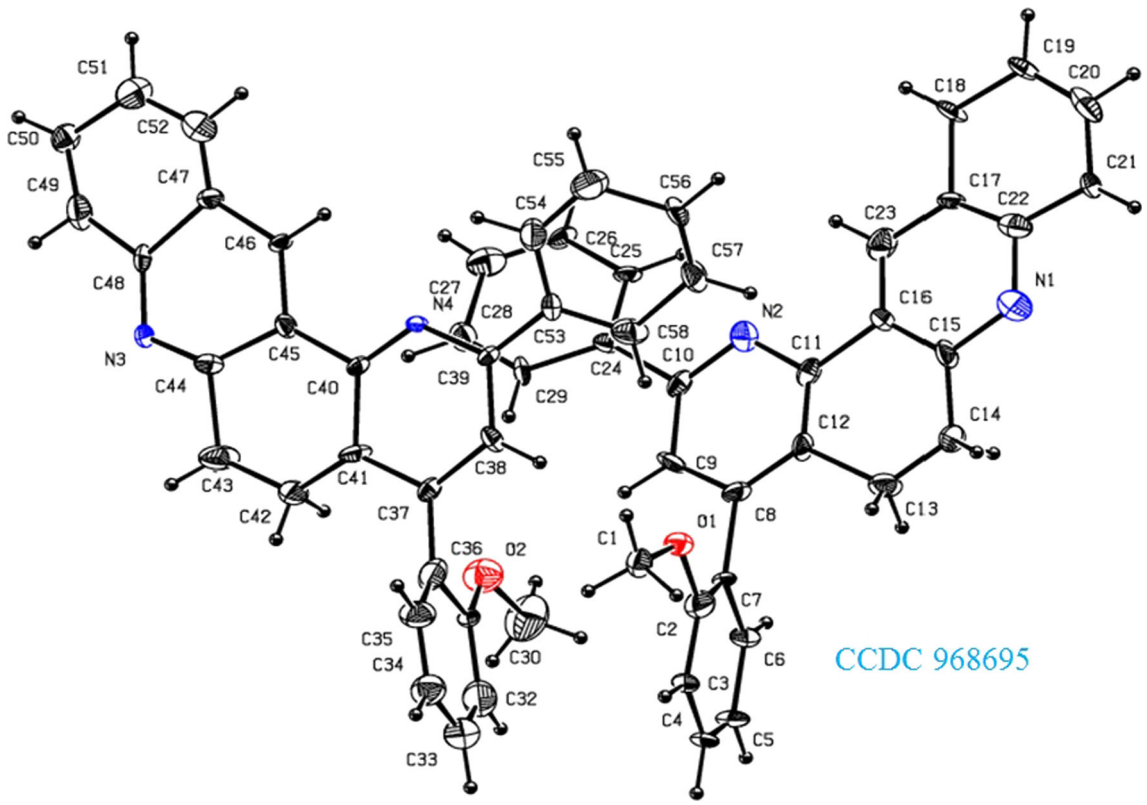
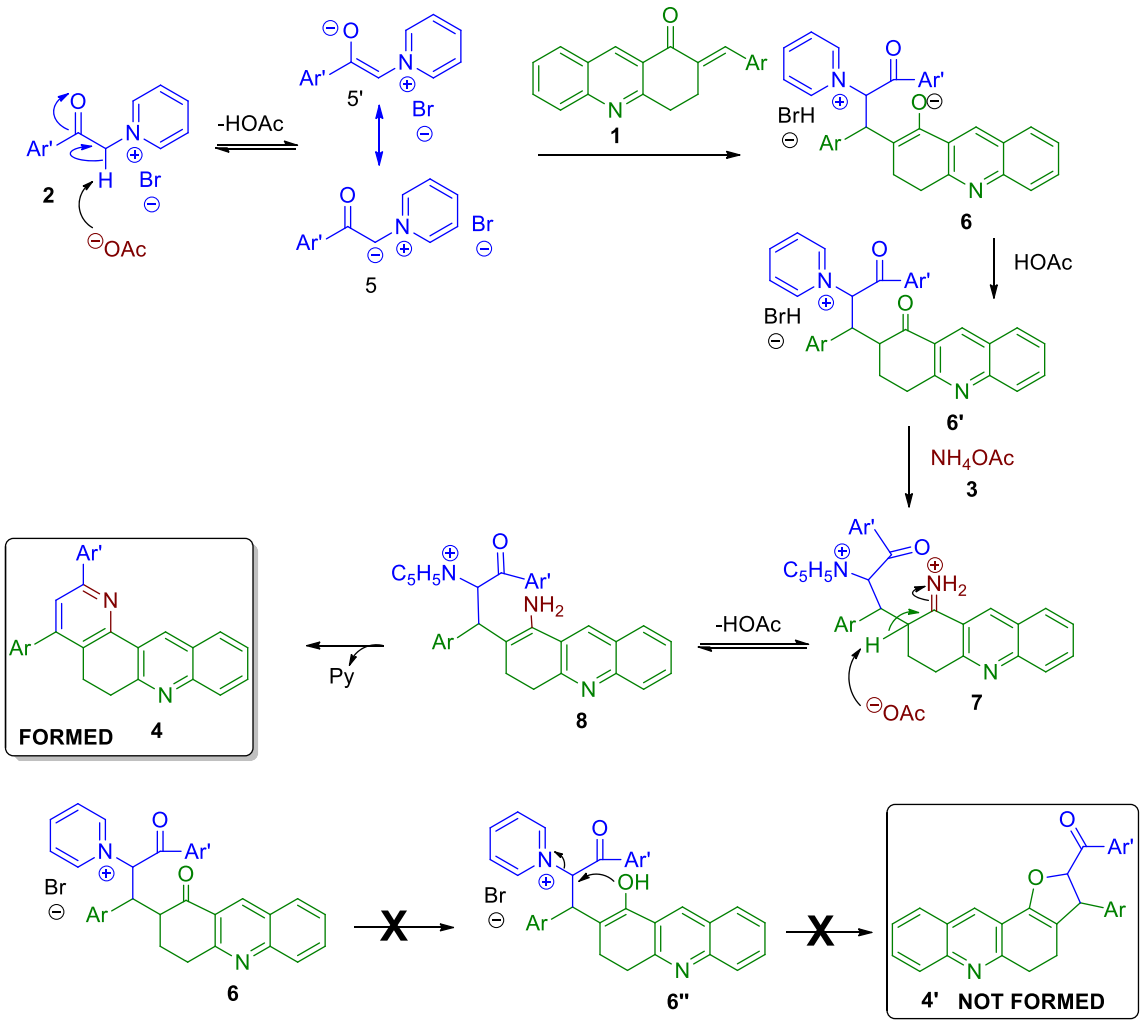


Fig. 3 ORTEP representation of **4g**

Chemical shifts are reported as δ values (ppm) (s = singlet; d = doublet; t = triplet; td = triplet of doublet; m = multiplet). All one- and two-dimensional NMR spectra were obtained using standard Bruker software throughout. Elemental analyses were performed on a PerkinElmer 2400 Series II Elemental CHN analyzer. Mass spectra were recorded on a LCQ Fleet mass spectrometer, Thermo Fisher Instruments Limited, USA. Electrospray ionization mass spectrometry (ESI–MS) analysis was performed in



Scheme 2 Proposed mechanism for the formation of **4**

the positive ion and negative ion modes on a liquid chromatography ion trap.

Single-crystal X-ray diffraction studies

Single crystals of 4-(2-methoxyphenyl)-2-phenyl-5,6-dihydrobenzo[j][1,7]phenanthroline **4g** were grown by slow evaporation solution growth method using ethanol as solvent at room temperature. Suitable crystals were selected for single-crystal X-ray diffraction studies. Single-crystal X-ray data set was collected on a Bruker AXS SMART APEX-2 diffractometer equipped with graphite monochromator. The structure was solved by direct methods and refined by full-matrix least-squares calculations using SHELXL-2014. Crystallographic data (excluding structure factors) for compound **4g** in this manuscript have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number **4g** CCDC 968695. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: +44 (0)1223-336033 or e-mail:deposit@ccdc.cam.ac.uk].

General procedure for the synthesis of 2,4-diaryl-5,6-dihydrobenzo[*j*][1,7]phenanthrolines 4

A mixture of 2-[arylmethylidene]-3,4-dihydro-1(2*H*)-acridinones (1 mmol), 1-(2-oxo-2-arylethyl)pyridin-1-ium bromide (1 mmol), and ammonium acetate (1.5 mmol) was heated under neat conditions at 110 °C for 6–9 h. After completion of the reaction (TLC monitoring), the mixture was poured onto ice water and the resulting solid was filtered and washed with water. This solid was recrystallized from ethanol to afford pure product **4**.

2,4-Di-*p*-tolyl-5,6-dihydrobenzo[*j*][1,7]phenanthroline (4a) Isolated as off white solid. Yield: 83%, m.p. = 227–228 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H: 2.45 (s, 3H, $-CH_3$), 2.46 (s, 3H, $-CH_3$), 3.12–3.17 (m, 2H), 3.24–3.29 (m, 2H),

7.34–7.36 (m, 6H, Ar–H), 7.55 (td, 1H, J = 7.8, 1.2 Hz, Ar–H), 7.64 (s, 1H, Ar–H), 7.72 (td, 1H, J = 7.8, 1.2 Hz Ar–H), 8.00–8.08 (m, 2H, Ar–H), 8.10 (d, 2H, J = 8.1 Hz, Ar–H), 9.27 (s, 1H, Ar–H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C: 21.1, 21.2, 24.7, 31.9, 120.4, 125.9, 126.7, 127.8, 128.1, 128.3, 128.5, 128.6, 128.9, 129.2, 129.4, 129.7, 132.5, 135.9, 136.5, 138.0, 138.8, 147.7, 149.7, 151.0, 155.2, 159.2; ESI–MS *m*/*z*, calcd: 412.19; found: 413.31 [M + 1]; anal. calcd for $C_{30}H_{24}N_2$: C, 87.35; H, 5.86; N, 6.79%. Found C, 87.49; H, 5.74; N, 6.89%.

2-(4-Methoxyphenyl)-4-*p*-tolyl-5,6-dihydrobenzo[*j*][1,7]phenanthroline (4b) Isolated as off white solid. Yield: 84%, m.p. = 198–200 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H: 2.46 (s, 3H, –CH_3), 3.11–3.16 (m, 2H), 3.24–3.29 (m, 2H), 3.90 (s, 3H, –OCH_3), 7.06 (d, 2H, J = 8.7 Hz, Ar–H), 7.34 (s, 4H, Ar–H), 7.55 (t, 1H, J = 7.5 Hz, Ar–H), 7.61 (s, 1H, Ar–H), 7.72 (td, 1H, J = 7.8, 1.5 Hz, Ar–H), 8.01 (d, 1H, J = 7.8 Hz, Ar–H), 8.06 (d, 1H, J = 8.7 Hz, Ar–H), 8.17 (d, 2H, J = 8.7 Hz, Ar–H), 9.25 (s, 1H, Ar–H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C: 21.3, 24.7, 32.1, 55.4, 114.1, 120.0, 126.0, 127.5, 128.1, 128.4, 128.7, 128.9, 129.2, 129.8, 132.0, 132.5, 136.0, 138.1, 147.8, 149.7, 151.0, 154.9, 159.3, 160.5; anal. calcd for $C_{30}H_{24}N_2O$: C, 84.08; H, 5.65; N, 6.54%. Found C, 84.00; H, 5.71; N, 6.58%.

2-Phenyl-4-*p*-tolyl-5,6-dihydrobenzo[*j*][1,7]phenanthroline (4c) Isolated as off white solid. Yield: 81%, m.p. = 205–206 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H: 2.47 (s, 3H, –CH_3), 3.13–3.17 (m, 2H), 3.25–3.30 (m, 2H), 7.34 (s, 4H, Ar–H), 7.46–7.48 (m, 1H, Ar–H), 7.52–7.57 (m, 3H, Ar–H), 7.67 (s, 1H, Ar–H), 7.72 (td, 1H, J = 7.8, 1.2 Hz, Ar–H), 8.01 (d, 1H, J = 8.1 Hz, Ar–H), 8.07 (d, 1H, J = 8.4 Hz, Ar–H), 8.21 (d, 2H, J = 7.2 Hz, Ar–H), 9.27 (s, 1H, Ar–H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C: 21.1, 24.7, 32.0, 120.7, 126.0, 126.8, 128.0, 128.1, 128.4, 128.6, 128.7, 128.8, 128.9, 129.2, 129.7, 132.5, 135.9, 138.1, 139.3, 147.9, 149.8, 151.2, 155.2, 159.2; ESI–MS *m*/*z*, calcd: 398.18; found: 399.29 [M + 1]; anal. calcd for $C_{29}H_{22}N_2$: C, 87.41; H, 5.56; N, 7.03%. Found C, 87.54; H, 5.67; N, 6.94%.

2-(4-Fluorophenyl)-4-*p*-tolyl-5,6-dihydrobenzo[*j*][1,7]phenanthroline (4d) Isolated as off white solid. Yield: 79%, m.p. = 218–220 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H: 2.46 (s, 3H, –CH_3), 3.13–3.17 (m, 2H), 3.25–3.29 (m, 2H), 7.19–7.26 (m, 2H, Ar–H), 7.34 (s, 4H, Ar–H), 7.55 (t, 1H, J = 7.2 Hz, Ar–H), 7.62 (s, 1H, Ar–H), 7.73 (t, 1H, J = 7.8 Hz, Ar–H), 8.01 (d, 1H, J = 8.1 Hz, Ar–H), 8.06 (d, 1H, J = 8.1 Hz, Ar–H), 8.19 (dd, 2H, J = 8.7, 5.4 Hz, Ar–H), 9.24 (s, 1H, Ar–H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C: 21.3, 24.8, 32.1, 115.5, 115.8, 120.5, 126.2, 128.1, 128.2, 128.5, 128.6, 128.7, 129.3, 130.0, 132.6, 135.5, 135.8, 138.3, 147.9, 150.0, 151.3, 154.3, 159.3; anal. calcd for $C_{29}H_{21}FN_2$: C, 83.63; H, 5.08; N, 6.73%. Found C, 83.70; H, 5.03; N, 6.69%.

2-(4-Nitrophenyl)-4-*p*-tolyl-5,6-dihydrobenzo[*j*][1,7]phenanthrolines (4e) Isolated as off white solid. Yield: 76%, m.p. = 238–240 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H: 2.47 (s, 3H, –CH_3), 3.16–3.20 (m, 2H), 3.26–3.20 (m, 2H), 7.35 (s, 4H, Ar–H), 7.57 (t, 1H, J = 7.2 Hz, Ar–H), 7.73 (s, 1H, Ar–H), 7.74–7.77 (m, 1H, Ar–H), 8.03 (d, 1H, J = 8.1 Hz, Ar–H), 8.07 (d, 1H, J = 8.4 Hz, Ar–H), 8.38–8.41 (m, 4H, Ar–H), 9.23 (s, 1H, Ar–H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C: 21.2, 24.8, 31.8, 121.2, 123.9, 126.2, 127.4, 127.9, 128.2, 128.5, 128.6, 129.3, 129.8, 130.0, 132.6, 135.3, 138.5, 145.1, 148.0, 148.1, 150.2, 151.8, 152.4, 158.9; ESI–MS *m*/*z*, calcd: 443.16; found: 444.27 [M + 1]; anal. calcd for $C_{29}H_{21}N_3O_2$: C, 78.54; H, 4.77; N, 9.47%. Found C, 78.42; H, 4.91; N, 9.42%.

4-(2-Methoxyphenyl)-2-(4-methoxyphenyl)-5,6-dihydrobenzo[j][1,7]phenanthroline (4f) Isolated as off white solid. Yield: 77%, m.p. = 235–236 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H: 2.81–2.90 (m, 1H), 2.99–3.09 (m, 1H), 3.22–3.29 (m, 2H), 3.81 (s, 3H, –OCH_3), 3.90 (s, 3H, –OCH_3), 7.04–7.08 (m, 3H, Ar–H), 7.11 (td, 1H, J = 7.2, 0.9 Hz, Ar–H), 7.30 (dd, 1H, J = 7.5, 1.8 Hz, Ar–H), 7.46 (td, 1H, J = 7.8, 1.5 Hz, Ar–H), 7.54 (td, 1H, J = 7.5, 0.9 Hz, Ar–H), 7.58 (s, 1H, Ar–H), 7.71 (td, 1H, J = 7.5, 1.5 Hz, Ar–H), 8.01 (d, 1H, J = 7.2 Hz, Ar–H), 8.06 (d, 1H, J = 8.4 Hz, Ar–H), 8.16 (d, 2H, J = 9.0 Hz, Ar–H), 9.26 (s, 1H, Ar–H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C: 24.4, 31.9, 55.3, 110.8, 114.0, 120.6, 120.8, 126.0, 127.8, 128.1, 128.3, 128.6, 129.0, 129.7, 129.8, 130.4, 132.1, 132.3, 146.9, 147.7, 150.3, 154.8, 156.4, 159.6, 160.3; anal. calcd for $C_{30}H_{24}N_2O_2$: C, 81.06; H, 5.44; N, 6.30%. Found C, 80.93; H, 5.38; N, 6.34%.

4-(2-Methoxyphenyl)-2-phenyl-5,6-dihydrobenzo[*j*][1,7]phenanthroline (4g) Isolated as off white solid. Yield: 82%, m.p. = 235–236 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ_H: 2.73–2.78 (m, 1H), 2.89–2.91 (m, 1H), 3.14 (m, 2H), 3.76 (s, 3H, –OCH_3), 7.09–7.19 (m, 2H,Ar–H), 7.24 (d, 1H, J = 7.2 Hz, Ar–H), 7.46–7.60 (m, 5H, Ar–H), 7.71–7.76 (m, 2H,Ar–H), 7.97 (d, 1H, J = 8.1 Hz, Ar–H), 8.17 (d, 1H, J = 8.1 Hz, Ar–H), 8.29 (d, 2H, J = 7.2 Hz, Ar–H), 9.25 (s, 1H, Ar–H); ^{13}C NMR (75 MHz, DMSO-d_6) δ_C: 24.6, 31.6, 55.9, 111.8, 121.2, 121.5, 126.7, 127.2, 127.3, 128.0, 128.6, 128.7, 129.2, 129.3, 129.5, 130.3, 130.5, 130.6, 130.8, 132.2, 139.0, 147.6, 147.8, 150.4, 154.6, 156.5, 159.6; anal. calcd for $C_{29}H_{22}N_2O$: C, 84.03; H, 5.35; N, 6.76%. Found C, 83.93; H, 5.47; N, 6.84%.

2-(4-Fluorophenyl)-4-(2-methoxyphenyl)-5,6-dihydrobenzo[*j*][1,7]phenanthroline (4 h) Isolated as off white solid. Yield: 78%, m.p. = 245–247 °C; ^{1}H NMR

(300 MHz, $CDCl_3$) δ_H: 2.85–2.92 (m, 1H), 3.00–3.11 (m, 1H), 3.23–3.30 (m, 2H), 3.82 (s, 3H, $-OCH_3$), 7.05 (d, 1H, J = 8.1 Hz, Ar–H), 7.11 (t, 1H, J = 7.5 Hz, Ar–H), 7.18–7.24 (m, 2H, Ar–H), 7.29 (dd, 1H, J = 7.5, 1.5 Hz, Ar–H), 7.47 (td, 1H, J = 7.5, 1.8 Hz, Ar–H), 7.55 (t, 1H, J = 7.5 Hz, Ar–H), 7.59 (s, 1H, Ar–H), 7.72 (td, 1H, J = 7.5, 1.5 Hz, Ar–H), 8.01 (d, 1H, J = 8.1 Hz, Ar–H), 8.06 (d, 1H, J = 8.4 Hz, Ar–H), 8.17–8.21 (m, 2H, Ar–H), 9.25 (s, 1H, Ar–H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C: 24.6, 31.9, 55.4, 110.9, 115.4, 115.7, 120.9, 121.0, 126.0, 127.7, 128.1, 128.5, 128.6, 128.7, 128.9, 129.8, 129.9, 130.4, 132.4, 135.7, 147.2, 147.9, 150.7, 154.1, 156.4, 159.5, 163.5 ($^1J_{C-F}$ = 246.5); ESI–MS m/z, calcd: 432.16; found: 433.25[M + 1]; anal. calcd for $C_{29}H_{21}FN_2O$: C, 80.54; H, 4.89; N, 6.48%. Found C, 80.61; H, 5.03; N, 6.43%.

2-(4-Chlorophenyl)-4-(2-methoxyphenyl)-5,6-dihydrobenzo[*j*][1,7]phenanthroline (4i) Isolated as off white solid. Yield: 85%, m.p. = 224–226 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H: 2.83–2.92 (m, 1H), 3.01–3.11 (m, 1H), 3.23–3.30 (m, 2H), 3.81 (s, 3H, $-OCH_3$), 7.05 (d, 1H, J = 8.4 Hz, Ar–H), 7.12 (t, 1H, J = 7.5 Hz, Ar–H), 7.28 (t, 1H, J = 7.5 Hz, Ar–H), 7.44–7.52 (m, 1H, Ar–H), 7.49 (d, 2H, J = 8.7 Hz, Ar–H), 7.55 (t, 1H, J = 7.5 Hz, Ar–H), 7.61 (s, 1H, Ar–H), 7.72 (t, 1H, J = 7.8 Hz, Ar–H), 8.01 (d, 1H, J = 8.1 Hz, Ar–H), 8.06 (d, 1H, J = 8.4 Hz, Ar–H), 8.15 (d, 2H, J = 8.4 Hz, Ar–H), 9.24 (s, 1H, Ar–H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C: 24.6, 31.9, 55.4, 110.9, 111.0, 120.9, 121.1, 126.1, 127.7, 128.1, 128.5, 128.7, 128.8, 129.8, 130.0, 130.2, 130.4, 132.4, 134.9, 137.9, 147.2, 150.8, 153.9, 156.4, 159.4; ESI–MS m/z, calcd: 448.13; Found: 449.25 [M + 1]; anal. calcd for $C_{29}H_{21}ClN_2O$: C, 77.58; H, 4.71; N, 6.24%. Found C, 77.44; H, 4.64; N, 6.29%.

4-(4-Chlorophenyl)-2-(4-fluorophenyl)-5,6-dihydrobenzo[*j*][1,7]phenanthroline (4j) Isolated as off white solid. Yield: 86%, m.p. = 213–214 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H: 3.08–3.13 (m, 2H), 3.25–3.30 (m, 2H), 7.19–7.27 (m, 2H, Ar–H), 7.37 (d, 2H, J = 8.4 Hz, Ar–H), 7.50 (d, 2H, J = 8.4 Hz, Ar–H), 7.55–7.58 (m, 1H, Ar–H), 7.58 (s, 1H, Ar–H), 7.73 (t, 1H, J = 7.2 Hz, Ar–H), 8.00 (d, 1H, J = 8.1 Hz, Ar–H), 8.06 (d, 1H, J = 8.1 Hz, Ar–H), 8.19 (dd, 2H, J = 8.7, 5.4 Hz, Ar–H), 9.23 (s, 1H, Ar–H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C: 24.6, 31.8, 115.5, 115.8, 120.0, 126.1, 127.8, 127.9, 128.4, 128.5, 128.6, 128.8, 130.0, 132.6, 134.5, 135.1, 137.0, 147.9, 148.6, 151.4, 154.3, 158.9, 163.6 ($^1J_{C-F}$ = 247.0); anal. calcd for $C_{28}H_{18}ClFN_2$: C, 76.97; H, 4.15; N, 6.41%. Found C, 77.09; H, 4.05; N, 6.49%.

4-(4-Bromophenyl)-2-*p*-tolyl-5,6-dihydrobenzo[*j*][1,7]phenanthroline (4k) Isolated as off white solid. Yield: 87%, m.p. = 222–223 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H: 2.45 (s, 3H, $-CH_3$), 3.08–3.12 (m, 2H), 3.25–3.30 (m, 2H), 7.30–7.36 (m, 4H, Ar–H), 7.57 (t, 1H, J = 7.2 Hz, Ar–H), 7.60 (s, 1H, Ar–H), 7.65 (d, 2H, J = 8.4 Hz, Ar–H), 7.73 (t, 1H, J = 7.2 Hz, Ar–H), 8.00–8.05 (m, 2H, Ar–H), 8.09 (d, 2H, J = 8.4 Hz, Ar–H), 9.26 (s, 1H, Ar–H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C: 21.3, 24.7, 32.0, 120.0, 122.6, 126.1, 126.7, 127.5, 128.0, 128.4, 128.6, 128.8, 129.5, 129.9, 130.4, 131.8, 132.7, 136.2, 137.7, 139.1, 147.9, 148.5, 151.3, 155.4, 159.0; ESI–MS m/z, calcd: 476.09; found: 477.22 [M + 1]; anal.calcd for $C_{29}H_{21}BrN_2$: C, 72.96; H, 4.43; N, 5.87%. Found C, 73.02; H, 4.56; N, 5.91%.

4-(4-Bromophenyl)-2-(4-methoxyphenyl)-5,6-dihydrobenzo[*j*][1,7]phenanthroline (4l) Isolated as off white solid. Yield: 83%, m.p. = 222–223 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H: 3.06–3.10 (m, 2H), 3.24–3.29 (m, 2H), 3.90 (s, 3H, $-OCH_3$), 7.06 (d, 2H, J = 8.7 Hz, Ar–H), 7.31 (d, 2H, J = 8.1 Hz, Ar–H), 7.52–7.57 (m, 2H, Ar–H), 7.65 (d, 2H, J = 8.1 Hz, Ar–H), 7.72 (t, 1H, J = 7.2 Hz, Ar–H), 8.00 (d, 1H, J = 8.1 Hz, Ar–H), 8.06 (d, 1H, J = 8.4 Hz, Ar–H), 8.16 (d, 2H, J = 8.4 Hz, Ar–H), 9.24 (s, 1H, Ar–H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C: 24.6, 31.8, 55.4, 114.2, 119.4, 123.1, 123.7, 126.2, 126.9, 128.0, 128.2, 128.4, 128.5, 128.7, 129.6, 130.0, 131.4, 132.7, 134.7, 140.6, 148.0, 148.5, 151.6, 155.4, 158.8; anal. calcd for $C_{29}H_{21}BrN_2O$: C, 70.59; H, 4.29; N, 5.68%. Found C, 70.50; H, 4.40; N, 5.61%.

4-(4-Bromophenyl)-2-phenyl-5,6-dihydrobenzo[*j*][1,7]phenanthroline (4m) Isolated as off white solid. Yield: 81%, m.p. = 227–228 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H: 3.05–3.07 (m, 2H), 3.22–3.24 (m, 2H), 7.27 (d, 2H, J = 7.8 Hz, Ar–H), 7.46–7.54 (m, 4H, Ar–H), 7.59 (s, 1H, Ar–H), 7.63 (d, 2H, J = 7.8 Hz, Ar–H), 7.70 (t, 1H, J = 7.5 Hz, Ar–H), 7.96 (d, 1H, J = 7.8 Hz, Ar–H), 8.06 (d, 1H, J = 8.1 Hz, Ar–H), 8.19 (d, 2H, J = 7.2 Hz, Ar–H), 9.22 (s, 1H, Ar–H);^{13}C NMR (75 MHz, $CDCl_3$) δ_C: 24.7, 31.9, 120.3, 122.6, 126.1, 126.9, 127.8, 128.0, 128.5, 128.8, 129.1, 129.9, 130.4, 131.8, 132.7, 137.7, 139.1, 148.0, 148.6, 151.5, 155.4, 159.0; ESI–MS m/z, calcd: 462.07; found: 463.27 [M + 1]; anal. calcd for $C_{28}H_{19}BrN_2$: C, 72.58; H, 4.13; N, 6.05%. Found C, 72.72; H, 4.01; N, 6.00%.

4-(4-Bromophenyl)-2-(4-chlorophenyl)-5,6-dihydrobenzo[*j*][1,7]phenanthroline (4n) Isolated as off white solid. Yield: 88%, m.p. = 204–206 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H: 3.09–3.13 (m, 2H), 3.26–3.30 (m, 2H), 7.31 (d, 2H, J = 8.4 Hz, Ar–H), 7.51 (d, 2H, J = 8.4 Hz, Ar–H), 7.56–7.59 (m, 1H, Ar–H), 7.59 (s, 1H, Ar–H), 7.66 (d, 2H, J = 8.4 Hz, Ar–H), 7.74 (t, 1H, J = 7.2 Hz, Ar–H), 8.01 (d, 1H, J = 8.1 Hz, Ar–H), 8.07 (d, 1H, J = 8.1 Hz, Ar–H), 8.14 (d, 2H, J = 8.4 Hz, Ar–H),

9.23 (s, 1H, Ar–H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C: 24.7, 31.9, 120.0, 122.8, 126.3, 128.0, 128.1, 128.4, 128.5, 128.8, 129.0, 130.1, 130.4, 131.9, 132.7, 135.3, 137.4, 137.5, 148.0, 148.7, 151.6, 154.1, 158.9; anal. calcd for $C_{28}H_{18}BrClN_2$: C, 67.56; H, 3.64; N, 5.63%. Found C, 67.68; H, 3.59; N, 5.55%.

4-(3-Nitrophenyl)-2-*p*-tolyl-5,6-dihydrobenzo[*j*][1,7]phenanthroline (4o) Isolated as off white solid. Yield: 76%, m.p. = 276–278 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H: 2.45 (s, 3H, $-CH_3$), 3.07–3.11 (m, 2H), 3.27–3.31 (m, 2H), 7.36 (d, 2H, J = 8.1 Hz, Ar–H), 7.56 (t, 1H, J = 7.5 Hz, Ar–H), 7.63 (s, 1H, Ar–H), 7.68–7.79 (m, 3H, Ar–H), 8.01 (d, 1H, J = 7.8 Hz, Ar–H), 8.06 (d, 1H, J = 8.4 Hz, Ar–H), 8.11 (d, 2H, J = 8.1 Hz, Ar–H), 8.33–8.36 (m, 2H, Ar–H), 9.27 (s, 1H, Ar–H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C: 21.3, 24.6, 31.7, 119.9, 123.1, 123.7, 126.2, 126.7, 127.3, 128.0, 128.3, 128.4, 128.7, 129.5, 129.6, 130.0, 132.8, 134.7, 135.9, 139.3, 140.5, 147.1, 147.9, 148.3, 151.6, 155.7, 158.7; anal. calcd for $C_{29}H_{21}N_3O_2$: C, 78.54; H, 4.77; N, 9.47%. Found C, 78.47; H, 4.81; N, 9.42%.

2-(4-Fluorophenyl)-4-(3-nitrophenyl)-5,6-dihydrobenzo[*j*][1,7]phenanthroline (4p) Isolated as off white solid. Yield: 80%, m.p. = 245–247 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H: 3.08–3.13 (m, 2H), 3.27–3.32 (m, 2H), 7.25 (d, 2H, J = 8.4 Hz, Ar–H), 7.57 (t, 1H, J = 7.5 Hz, Ar–H), 7.61 (s, 1H, Ar–H), 7.70–7.79 (m, 3H, Ar–H), 8.02 (d, 1H, J = 8.1 Hz, Ar–H), 8.07 (d, 1H, J = 8.4 Hz, Ar–H), 8.20 (dd, 2H, J = 8.7, 5.4 Hz, Ar–H), 8.34–8.37 (m, 2H, Ar–H), 9.25 (s, 1H, Ar–H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C: 24.6, 31.7, 115.7, 119.8, 123.1, 123.6, 126.2, 127.6, 127.9, 128.1, 128.4, 128.5, 128.6, 128.7, 129.6, 130.1, 132.7, 134.6, 134.8, 140.3, 147.3, 148.0, 148.4, 151.8, 156.6, 163.7($^1J_{C-F}$ = 247.1); anal. calcd for $C_{28}H_{18}FN_3O_2$: C, 75.16; H, 4.05; N, 9.39%. Found C, 75.29; H, 3.96; N, 9.28%.

2-(4-Chlorophenyl)-4-(3-nitrophenyl)-5,6-dihydrobenzo[*j*][1,7]phenanthroline (4q) Isolated as off white solid. Yield: 77%, m.p. = 244–246 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H: 3.09–3.14 (m, 2H), 3.28–3.33 (m, 2H), 7.52 (d, 2H, J = 8.7 Hz, Ar–H), 7.57 (t, 1H, J = 7.5 Hz, Ar–H), 7.63 (s, 1H, Ar–H), 7.71–7.80 (m, 3H, Ar–H), 8.03 (d, 1H, J = 8.1 Hz, Ar–H), 8.07 (d, 1H, J = 8.4 Hz, Ar–H), 8.16 (d, 2H, J = 8.4 Hz, Ar–H), 8.34–8.38 (m, 2H, Ar–H), 9.25 (s, 1H, Ar–H); ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO-d_6) δ_C: 24.1, 31.1, 119.6, 122.8, 123.1, 125.8, 127.4, 127.6, 127.7, 127.8, 128.3, 128.4, 129.4, 129.7, 132.3, 134.4, 134.7, 136.7, 139.6, 147.0, 147.4, 147.8, 153.8, 158.2; anal. calcd for $C_{28}H_{18}ClN_3O_2$: C, 72.49; H, 3.91; N, 9.06%. Found C, 72.62; H, 3.80; N, 9.15%.

4-(3-Nitrophenyl)-2-phenyl-5,6-dihydrobenzo[*j*][1,7]phenanthroline (4r) Isolated as off white solid. Yield: 75%, m.p. = 231–232 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H: 3.09–3.13 (m, 2H), 3.28–3.33 (m, 2H), 7.49–7.59 (m, 4H, Ar–H), 7.66 (s, 1H, Ar–H), 7.70–7.80 (m, 3H, Ar–H), 8.02 (d, 1H, J = 8.1 Hz, Ar–H), 8.07 (d, 1H, J = 8.4 Hz, Ar–H), 8.21 (d, 2H, J = 7.2 Hz, Ar–H), 8.35–8.37 (m, 2H, Ar–H), 9.28 (s, 1H, Ar–H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C: 24.6, 31.7, 120.1, 123.1, 123.6, 126.1, 126.8, 127.6, 128.0, 128.3, 128.5, 128.6, 128.7, 129.2, 129.6, 130.0, 132.8, 134.6, 138.7, 140.5, 147.2, 148.0, 148.4, 151.7, 155.7, 158.6; anal. calcd for $C_{28}H_{19}N_3O_2$: C, 78.31; H, 4.46; N, 9.78%. Found C, 78.42; H, 4.52; N, 9.69%.

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References

1. Anastas PT, Kirchhoff MM (2002) Origins, current status, and future challenges of green chemistry. Acc Chem Res 35:686–694. https://doi.org/10.1021/ar010065m
2. Anastas PT, Warner JC (1998) Green chemistry: theory and practice. Oxford University Press, New York, p 30
3. Tanaka K, Toda F (2000) Solvent-free organic synthesis. Chem Rev 100:1025–1074. https://doi.org/10.1021/cr940089p
4. Gawande MB, Bonifácio VDB, Luque R, Branco PS, Varma RS (2014) Solvent-free and catalysts-free chemistry: a benign pathway to sustainability. Chemsuschem 7:24–44. https://doi.org/10.1002/cssc.201300485
5. Tietze LF, Modi A (2000) Multicomponent domino reactions for the synthesis of biologically active natural products and drugs. Med Res Rev 20:304–322. https://doi.org/10.1002/1098-1128(200007)20
6. Tietze LF (1996) Domino reactions in organic synthesis. Chem Rev 96:115–136. https://doi.org/10.1021/cr950027e
7. Pellissier H (2013) Stereocontrolled domino reactions. Chem Rev 113:442–524. https://doi.org/10.1021/cr300271k
8. Tietze LF, Brasche G, Gericke K (2006) Domino reactions in organic synthesis. Wiley, Weinheim. ISBN 3-527-29060-5
9. Dömling A, Wang W, Wang K (2012) Chemistry and biology of multicomponent reactions. Chem Rev 112:3083–3135. https://doi.org/10.1021/cr100233r
10. Ruijter E, Scheffelaar R, Orru RVA (2011) Multicomponent Reaction design in the quest for molecular complexity and diversity. Angew Chem Int Ed 50:6234–6246. https://doi.org/10.1002/anie.201006515
11. Zhu J, Bienaymé H (2005) Multicomponent reaction. Wiley, Weinheim. ISBN 978-3-527-30806-4
12. Singh MS, Chowdhury S (2012) Recent developments in solvent-free multicomponent reactions: a perfect synergy for eco-compatible organic synthesis. RSC Adv 2:4547–4592. https://doi.org/10.1039/C2RA01056A
13. Kumar S, Bawa S, Gupta H (2009) Biological activities of quinoline derivatives. Mini Rev Med Chem 9:1648–1654. https://doi.org/10.2174/138955709791012247
14. Roth HJ, Kleemann A (1988) Drug synthesis, in pharmaceutical chemistry, vol I. Wiley, New York. ISBN 0470210370

15. Schmitz FJ, DeGuzman FS, Hossain ME, van der Helm D (1991) Cytotoxic aromatic alkaloids from the ascidian *Amphicarpa meridiana* and *Leptoclinides* sp.: meridine and 11-hydroxyascididemin. J Org Chem 56:804–808. https://doi.org/10.1021/jo00002a055
16. Delfourne E, Kiss R, Le Corre L, Dujols F, Bastide J, Collignon F, Lesur B, Frydman A, Darro F (2004) Synthesis and in vitro antitumor activity of ring C and D-substituted phenanthrolin-7-one derivatives, analogues of the marine pyridoacridine alkaloids ascididemin and meridine. Bioorg Med Chem 12:3987–3994. https://doi.org/10.1016/j.bmc.2004.06.006
17. Delfourne E, Darro F, Subielos NB, Decaestecker C, Bastide J, Frydman A, Kiss R (2001) Synthesis and characterization of the antitumor activities of analogues of meridine, a marine pyridoacridine alkaloid. J Med Chem 44:3275–3282. https://doi.org/10.1021/jm0108496
18. Hu YZ, Zhang G, Thummel RP (2003) Friedländer approach for the incorporation of 6-bromoquinoline into novel chelating ligands. Org Lett 5:2251–2253. https://doi.org/10.1021/ol034559q
19. Cucciolito ME, Vitagliano A (1992) Selective stabilization of the anti isomer of (η^3-allyl)palladium and -platinum complexes. Organometallics 11:3954–3964. https://doi.org/10.1021/om00060a009
20. Albano G, Belser P, Cola LD, Gandolfi MT (1999) New luminescent ruthenium complexes with extended π systems. Chem Commun. https://doi.org/10.1039/A900911F
21. Groundwater PW, Solomons KR, Munawar AM (1996) Benzophenanthrolines and related fused acridines. Patent WO 1996018611 A2
22. Roopan SM, Bharathi A, Palaniraja J, Anand K, Gengan RM (2015) Unexpected regiospecific Michael addition product: synthesis of 5,6-dihydrobenzo[1,7] phenanthrolines. RSC Adv 5:38640–38645. https://doi.org/10.1039/C4RA16640J
23. Vivek Kumar S, Muthusaravanan S, Muthusubramanian S, Perumal S (2016) An efficient one pot three-component domino reaction for the synthesis of 1,3,4-trisubstituted pyrroles. ChemistrySelect 1:675–679. https://doi.org/10.1002/slct.201600108
24. Uma Rani G, Vivek Kumar S, Bharkavi C, Menendez JC, Perumal S (2016) One-pot access to a library of dispiro oxindole-pyrrolidine/pyrrolothiazole-thiochromane hybrids via three-component 1,3-dipolar cycloaddition reactions. ACS Comb Sci 18:337–342. https://doi.org/10.1021/acscombsci.6b00011
25. Vivek Kumar S, Muthusubramanian S, Perumal S (2015) Facile "on water" domino reactions for the expedient synthesis of 2H-thiopyrano[2,3-b]quinolones. RSC Adv 5:30826–30832. https://doi.org/10.1039/C5RA04795A
26. Vivek Kumar S, Muthusubramanian S, Perumal S (2015) A solvent- and catalyst-free domino reaction for the efficient synthesis of 3-arylthiazolidine-2-thiones under microwave irradiation. RSC Adv 5:90451–90456. https://doi.org/10.1039/C5RA19112B
27. Vivek Kumar S, Muthusubramanian S, Menéndez JC, Perumal S (2015) An efficient synthesis of N-substituted 3-nitrothiophen-2-amines. Beilstein J Org Chem 11:1707–1712. https://doi.org/10.3762/bjoc.11.185
28. Prasanna P, Balamurugan K, Perumal S, Menéndez JC (2011) A facile, three-component domino protocol for the microwave-assisted synthesis of functionalized naphtho[2,3-b]furan-4,9-diones in water. Green Chem 13:2123–2129. https://doi.org/10.1039/c0gc00952k
29. Gunasekaran P, Balamurugan K, Sivakumar S, Perumal S, Menéndez JC, Almansour AI (2012) Domino reactions in water: diastereoselective synthesis of densely functionalized indolyldihydrofuran derivatives. Green Chem 14:750–757. https://doi.org/10.1039/c2gc16517a
30. Indumathi S, Perumal S, Anbananthan N (2012) A facile eco-friendly three-component protocol for the regio- and stereoselective synthesis of functionalized trans-dihydrofuro[3,2-c]-quinolin-4(2H)-ones. Green Chem 14:3361–3367. https://doi.org/10.1039/c2gc36040c