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Unexpected regiospecific Michael addition Product: Synthesis of 5,6-dihydrobenzo[1,7] phenanthrolines

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The unexpected formation of 5,6-dihydrobenzo[1,7]phenanthroline instead of 5,6-dihydrobenzo[1,7]phenanthroline-3-carbonitrile has been observed in acridine molecules for the first time using Michael addition methodology. Moreover, we have identified Montmorillonite KSF clay as catalyst to offer regiospecific expected dihydrobenzo[1,7]phenanthroline-3-carbonitrile product and NaH base as regiospecific formation of unexpected Michael addition 5,6-dihydrobenzo[1,7]phenanthroline products. On the basis of systematic study, the novel regiospecificity could be assigned by utilization of suitable catalyst.

Introduction

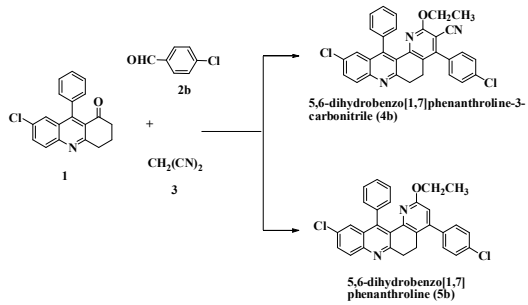
Heterocycles show a energetic part in agricultural, pharmacological, and synthetic fields. Subsequently, the progress of methodologies beneficial for the assembly of molecules containing heterocyclic templates. It remains to draw the consideration of both the academic and industrial societies. The investigation of the chemistry of acrinine has been one of the active area of heterocyclic chemistry.From an environmental and economic perception it is becoming observable that the old-fashioned methods of execution chemical synthesis are unsustainable and have to be altered. Organic reactions carried out through multicomponent reactions (MCR) is an eye-catching area of investigation in current organic synthesis.[1] MCR are convergent reactions, in which three or more precursor reacts to form a product. It has the tendency for the inherent formation of several bonds in one operation without isolating the intermediates. This strategies would allow the minimization of waste production. MCR is flexible reaction for the rapid generation of complex molecules with often biologically relevant scaffold structures.[1] In the manner that very significant research is often accomplished by multidisciplinary research teams. Multicomponent coupling reactions provide a solution since they are more efficient, cost effective and less wasteful than traditional methods. The realization of assembly multiple bonds in MCR promotes a sustainable approach to new molecule discovery. Preparation of an efficient functionalized heterocyclic compound is one of the important tasks in organic synthesis. MCR is one of the method which address the challenges for the development of eco-compatible reactions.[1] These MCR reaction has become one of the important methods for the rapid construction of heterocyclic compounds.[2,3] Unexpected chemical reactions reveal the new kind of chemical pathway and novel compounds in organic synthesis.[4-6] Literature survey reveals that the synthesis of pyridine and pyrimidine analogues can be achieved *via* Michael reactions.[7] Based on the literature survey, Michael addition forms only the presence of nitrile functional group in heterocyclic compounds.[8-11]In continuation of our earlier report in organic synthesis,[12-17] our current studies focused on multicomponent synthesis of heterocycles.[18] We were interested in the straightforward construction of 5,6-dihydrobenzo[1,7] phenanthroline-3-carbonitrile synthesis but at this juncture, we have found that there is an unexpected 5,6-dihydrobenzo[1,7]phenanthroline product. In continuation of this we herewith reported the optimization of reaction conditions to get regiospecific unexpected product as well as expected product.

Results & Discussion

The Michael addition reaction is broadly documented as one of the vital ***C-C*** bond forming reaction in organic synthesis and it can commonly be carried out with a strong base.[19] Though, the base catalysed method occasionally agonizes from drawbacks of incompatibility with base-sensitive functionality and side reactions, such as retro-Michael type decompositions and autocondensations. Even though these methods are appropriate for synthetic applications, several of these measures are associated with some hindrances such as toxic reagents, long duration, mind-numbing workup and low yeilds. Thus, progress of new methods using cheap and commercially available less toxic reagents to afford high yields of products in short reaction times are important. Literature reveals that Michael addition in presence of Et_3N[20], the reaction required long heating periods and the product yields were only mode rate and side products were formed[21]. To avoid such problems, recently substantial attention has been focused on the use of phase transfer catalysts, transition metal complexes, clay supported catalysts and Lewis acid catalysts such as $Yb(OTf)_3$, $ZrCl_4$, $BF_3.Et_2O$, $Bi(OTf)_3$, and trifluoromethane sulfonic acid in Michael additions.[22-27] In this investigation, MCR has been carried out by the following synthetic strategy. 7-chloro-9-phenyl-3,4- dihydroacridin-1(2*H*)-one **1** react with 4-choloro benzaldehyde **2** and malononitrile **3** were carried out with various base catalysts (**Table 1**) afforded the expected 10-chloro-4-(4-chlorophenyl)-2-ethoxy-12-phenyl-5,6-dihydrobenzo[*j*][1,7] phenanthroline – 3 -carbonitrile **4** and unexpected 10-chloro-4-(4-chloro phenyl)-2-ethoxy-12-phenyl-5,6-dihydrobenzo[*j*][1,7] phenanthroline **5.** The results are summarized in **Table 1**. Under the optimized reaction conditions, the base catalyst is varied from mild inorganic base to strong bases. The Michael reaction of β-functionalized or α,β-unsaturated carbonyls with malononitrile has been described. In table 1, optimization of base catalyst is summarized. The mild base K_2CO_3 in ethanol and water (1:1) medium yields (Table 1, Entry 3) the less amount of expected

compound **4** and trace amount of unexpected compound **5**. Further, increasing the order of base catalyst yields moderate amount of expected compound **4** (Table 1, Entry 4) and less amount of unexpected compound **5**.

Table 1. Effect of reaction conditions on the multicomponent reaction for the **4b** and **5b.**



Entry[a]	Base/Equiv	Solvent (1:1)	Yield (%)[b]	
			4a	5a
1	K_2CO_3/1	EtOH/water	-	-
2	K_2CO_3/3	EtOH/water	Trace[c]	-
3	K_2CO_3/5	EtOH/water	30	Trace[c]
4	K_2CO_3/10	EtOH/water	32	5
5	Na_2CO_3/10	EtOH/water	37	5
6	KOH/20	EtOH	53	9
7	NaOH/20	EtOH	55	17
8	Na/20	EtOH	57	19
9	NaH/5	EtOH	55	24
10	NaH/1	EtOH/benzene	43	27
11	NaH/2	EtOH/benzene	35	31
12	NaH/3	EtOH/benzene	23	39
13	NaH/4	EtOH/benzene	16	57
14	NaH/5	EtOH/benzene	10	68
15	NaH/6	EtOH/benzene	Trace[c]	73
16	**NaH/7**	**EtOH/benzene**	**Trace[c]**	**78**
17	NaH/8	EtOH/benzene	Trace[c]	78
18	KSF/100mg	EtOH	87	-
19	KSF200 mg	EtOH	88	-
20	**KSF/300mg**	**EtOH**	**90**	**-**
21	KSF/400mg	EtOH	90	-

[a] All reactions were carried out in 1 mmol of (1:1:1) equiv of reactants (**1**, **2a** and **3**) and 5 mL of solvent unless otherwise noted. [b]isolated yield, [c] TLC. The optimized conditions were mentioned by bold letters.

Our aim is to optimize the reaction conditions to get unexpected compound **5** regiospecifically. Depending on the base nature, the reaction conditions vary from mild base to strong base. A strong base NaH plays major role to get unexpected product **5** (Table 1, Entry 9). The solvents also influence the yield of the products. NaH in EtOH and benzene (1:1) ratio (**Table 1, Entry 10-17**) increase the yield of unexpected compound **5** and decrease the yield of expected compound **4**. The optimized conditions are NaH in EtOH/benzene (Table 1, Entry 16) have given 78 % of yield. Further increasing the amount of base, the yield percentage of the products was neither increased nor altered. Our result extend our intrest to get the expected Michael product **4** regiospecifically. In this concern, we have carried out the reaction using Montmorillonite KSF clay (KSF) as catalyst instead of the above mentioned bases (Table 1, Entries 18-21) which yields regiospecifically 5,6-dihydrobenzo[1,7]phenanthroline-3-carbonitrile **4**. The structure of compounds **4** and **5** were confirmed by ^{1}H NMR, ^{13}C NMR and mass spectrometry (Supporting Information). The unexpected compound **5b** was supported by X-ray crystallography **ORTEP** (**Figure 1**) diagram.

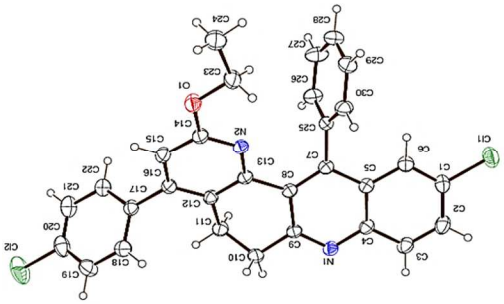
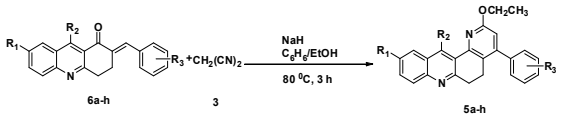


Figure 1. ORTEP for compound **5b**

Earlier in the literature, the Michael addition offered the expected carbonitrile product alone. Moreover, no literature reports were available for the absence of carbonitrile functional group in acridine systems. In this present study, our aim is to focus synthesis of regiospecific unexpected product **5** and expected compound **4** in various 5,6-dihydrophenthroline analogues. From our optimized condition (**Table 2**), we have utilized various (*E*)-2-benzylidene-7-chloro-9-phenyl-3,4-dihydroacridin-1(2*H*)-one derivatives **6a-h** were reacted with malononitrile **3** in presence of NaH as a strong base (Entry 15) to get regiospecific unexpected products **5a-h**. Physical data of all synthesized compounds **5a-h** are summarized in table 2.

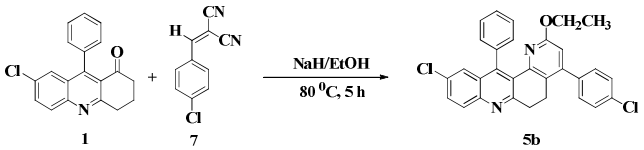
Table 2. Synthesis of 5,6-dihydrobenzo [1,7] phenanthrolines **5(a-h)**, (**5a-h**)



Entry	R_1	R_2	R_3	m.p. (°C)	Yield (%)[a]
5a	-Cl	$-C_6H_5$	3,4-OCH_3	142-144	81
5b	-Cl	$-C_6H_5$	4-Cl	236-238	79
5c	-H	$-C_6H_5$	4-Cl	163-165	80
5d	-H	$-CH_3$	4-Cl	195-197	76
5e	-Cl	$-C_6H_5$	2-Cl	160-162	75
5f	-Cl	$-C_6H_5$	2,5-OCH_3	138-140	78
5g	-Cl	$-C_6H_5$	3-OCH_3	146-148	75
5h	-Cl	$-C_6H_5$	H	150-152	75

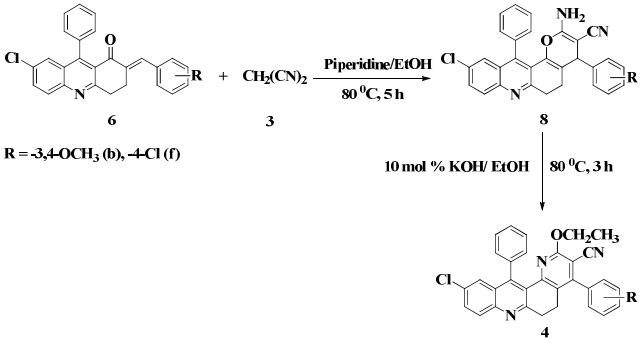
[a]Isolated yield

Further, we have investigated the substrate scope for the formation of the product with two transformations. The results are shown in further schemes and the regiochemical outcomes of the reactions are examined. The mode of addition reactions influences the organic transformation, solvent and catalyst.[28] In this concern, we have tried to get regiospecific 5,6-dihydrobenzo[1,7]phenanthroline **5** from 7-chloro-9-phenyl-3,4-dihydroacridin-1(2*H*)-one.We have synthesized an intermediate 2-(4-chlorobenzylidene)malononitrile **7** using 4-cholorobenzaldehyde **2** and malononitrile **3** in ethanol refluxed for 8 h. The intermediate **7** were further treated with 7-chloro-9-phenyl-3,4-dihydroacridin-1(2*H*)-one **1** using an optimized condition (entry 15) results that unexpected compound **5b** (**Scheme 1**).



Scheme 1. An alternative route for synthesis of 5,6-dihydrobenzo [1,7] phenanthroline, **5b**

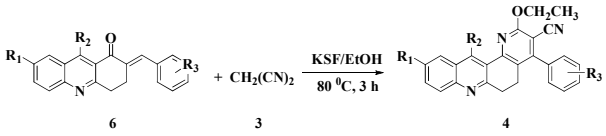
Another methodology has been attempted for the regiospecific preparation of expected 5,6-dihydrobenzo[1,7]phenanthroline-3-carbonitrile **4** (**Scheme 2**). However, these methods suffer from some limitations such as low yield, poor regioselectivity, number of steps and prolonged reaction time.[29]



Scheme 4. Synthesis of 5,6-dihydrobenzo [1,7] phenanthroline -3-carbonitriles *via* two steps

Therefore, we decided to develop a mild, economical and acomplementary synthetic approach. To overcome this problem we utilized Montmorillonite KSF clay as catalyst for a attempt (**Table 3**).

Table 3. Scope of various dihydrobenzo [1,7] phenan throline -3-carbonitriles **4(a-d)**



Entry	R_1	R_2	R_3	m.p. (°C)	Yield (%)[a]
4a	-Cl	$-C_6H_6$	3,4-OCH_3	162-164	81
4b	-Cl	$-C_6H_6$	4-Cl	210-212	78
4c	-H	$-C_6H_6$	4-Cl	231-233	81
4d	-H	$-CH_3$	4-Cl	230-232	72

[a]Isolated yield

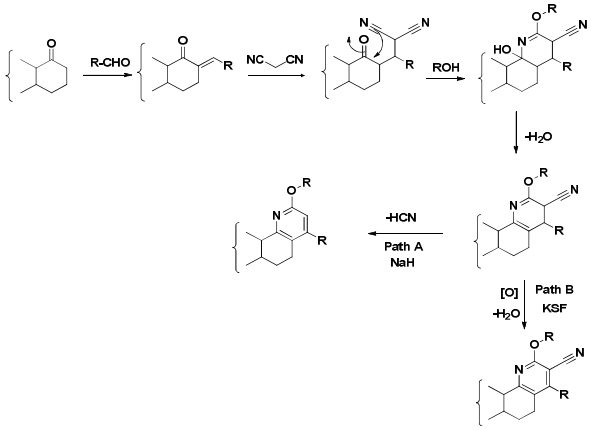
In this case (*E*)-2-benzylidene-7-chloro-9-phenyl-3,4-dihydroacridin-1(2*H*)-one **6** reacted with malononitrile **3** in presence of KSF as catalyst containing 10 mL of ethanol yields 5,6-dihydrobenzo[1,7] phenanthroline-3-carbonitrile **4.** The KSF as a catalyst for the optimized reaction conditions is represented in table 1. The reproducibility of catalyst is studied up to 3 cycles. The results are specified in **Table 3**.

The reproducibility of KSF catalyst was employed and we have been reported 3 consequtive cycles of the concern reaction **(Table 4).** After the reaction completion, the mixture was cooled to room temperature and poured into the ice water with continuous stirring. The solid was filtered and dissolved in dichloromethane. The catalyst was filtered to dryness and recycled for next rection cycle.

Table 4. Reproducibility of Montmorillonite KSF catalyst

Run	Amount (mg)	Yield (%)
1	250	90
2	230	89
3	220	88

A plausible reaction mechanism is proposed for the formation of expected 5,6-dihydrobenzo[1,7]phenanthroline-3-carbonitrile **4** (Path A) and unexpected 5,6-dihydrobenzo[1,7]phenanthroline **5** (Path B) on the basis of the results obtained in **Scheme 3**. Investigation of these two transformations are carried out as per the reported method using cyclohexanone and α- tetralone analogous.[10,11] The results reveals the corresponding carbonitrile functional group contains the expected Michael product.



Scheme 3. A plausible reaction mechanism for the formation of phenanthroline compounds, **4** and **5**

Conclusion

In conclusion, we have developed regiospecific synthesis of 5,6-dihydrobenzo[1,7]phenanthrolines **5** using NaH as base by Michael addition reaction. Expected 5,6-dihydrobenzo[1,7]phenanthroline-3-carbonitriles **4** was reported by using Montmorillonite KSF clay as catalyst. These data have lead to the development of an alternative and straight forward mechanistic pathway for Michael addition reaction. This report provides an easy method for direct access to regiospecific expected and unexpected compounds.

Experimental section

Purification of reaction products were carried out by chromatography using silica gel (200- 300 mesh). Melting points were measured on Elche Microprocessor based DT apparatus using an open capillary tube and are corrected with standard benzoic acid. FT-IR spectrum was recorded on a SHIMADZU Infrared spectrophotometer (400–4000 cm^{-1}; resolution: 1 cm^{-1}) using KBr

pellets. NMR spectra were in $CDCl_3$ or DMSO (^1H at 400 MHz and ^{13}C at 100 MHz) and data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), and coupling constant(s) in Hz. ESI-MS data were obtained using ESI-MS Thermo Fleet ionization. Unless otherwise noted, all reagents were obtained commercially and used without further purification.

Regiospecific synthesis of 5,6-dihydrobenzo [1,7] phenanthrolines 5(a-h)

A mixture of 4 equivalent (0.96 g) NaH was stirred with a solution contains 5 ml of ethanol and 5 ml of benzene in ice cold condition at 15 min. A mixture of corresponding (*E*)-2-benzylidene-7-chloro-9-phenyl-3,4-dihydroacridin-1(2*H*)-one, **6** (1 mmol) and malononitrile, **3** (1 mmol) were added with a solution contains NaH base. After addition of the reagents and reactants the reaction mixture was refluxed for 3 h at 80 ^{0}C. The reaction was monitored by TLC. After the completion of the reaction, the reaction mixture was poured into ice cold water and neutralized with 2N HCl. The precipitate was filtered and washed with water. The product was purified by column chromatography results that compound, **5**.

Regiospecific Synthesis of 5, 6-dihydrobenzo [1,7] phenanthroline-3-carbonitriles 4 (a-d)

A mixture of (*E*)-2-benzylidene-7-chloro-9-phenyl-3,4-dihydroacridin-1(2*H*)-one, **6** (1 mmol), malononitrile, **3** (1 mmol) KSF in ethanol (10 mL) were refluxed for 3 h. The completion of reaction was noted by TLC. Catalyst was recovered and reused for further three times. The product was purified by column chromatography. The result offered expected compound, **4.**

Spectral characterization of the synthesized compounds are listed below

10-chloro-4-(3,4-dimethoxyphenyl)-2-ethoxy-12-phenyl-5,6-dihydrobenzo[*j*][1,7] phenanthroline-3-carbonitrile (4a)

Orange solid; Yield 81 %; mp: 162-164 ˚C. FT-IR (KBr pellet) ν_{max}/(cm^{-1}): 2225 (CN), 1541, 1516 (C-O-C); ^1H NMR ($CDCl_3$): δ (ppm), 1.08 (t, *J* = 6.8 Hz, 3H), 2.98 (t, *J* = 6.8 Hz, 2H,), 3.17-3.29 (m, 4H), 3.90 (s, 3H), 3.94 (s, 3H), 6.51 (s, 1H), 6.88 (d, *J* = 8 Hz, 1H), 6.94 (d, *J* = 8 Hz, 2H), 7.29 (s, 1H), 7.39-7.48 (m, 4H), 7.59 (d, *J* = 8.8 Hz, 1H), 7.98 (d, *J* = 8.8 Hz,1H); ^{13}C NMR ($CDCl_3$): δ (ppm), 14.4, 24.5, 29.7, 56.0, 61.2,110.3, 110.9, 112.0, 121.9, 125.4, 125.8, 126.9, 128.0, 128.3, 129.2, 129.6, 130.1, 130.1, 131.2, 133.7, 138.8, 144.5, 145.4, 148.8, 149.0, 149.2, 151.1, 161.2, 161.3; EI-MS: m/z 548.58.

10-chloro-4-(4-chlorophenyl)-2-ethoxy-12-phenyl-5,6-dihydro benzo[*j*][1,7]phenanthroline-3-carbonitrile (4b):

Yellow solid; Yield 78 %; mp: 210-212 ˚C; FT-IR (KBr pellet) ν_{max}/(cm^{-1}): 2222 (CN), 1544, 1492 (C-O-C); ^1H NMR (400 MHz, $CDCl_3$) δ 1.12 (t, *J* = 14.4 Hz, 3H), 2.81 (t, *J* = 8.25 Hz, 2H,), 3.18 (t, *J* = 13.2 Hz, 2H), 3.31-3.36 (m, 2H,), 7.25-7.32 (m, 5H), 7.47-7.52 (m, 5H), 7.99 (d, *J* = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.1, 24.3, 33.5, 63.0, 115.0, 125.3, 125.5, 126.1, 127.4, 128.6, 129.0, 129.2, 129.5, 129.6, 130.1, 130.2, 130.6, 131.2, 132.3, 133.3, 135.8, 138.1, 146.0, 146.5, 153.3, 153.6, 160.5, 161.9; ESI-MS: m/z 522.23.

4-(4-Chloro-phenyl)-2-ethoxy-12-phenyl-5,6-dihydro-benzo[*j*][1,7] phenanthroline-3-carbonitrile (4c):

Pale yellow solid; Yield 81 %; mp: 231-233 ˚C; FT-IR (KBr pellet) ν_{max}/ ($cm^{-}1$): 2220(CN), 1545, 1495 (C-O-C); ^1H NMR (400 MHz, $CDCl_3$) δ 1.05 (t, *J* = 7.2 Hz, 3H,), 2.75 (t, *J* = 6.8 Hz, 2H,), 3.14 (t, *J* = 7.2 Hz, 2H), 3.32-3.30 (m, 2H), 7.31 (d, *J* = 6.8 Hz, 2H), 7.41-7.57 (m, 7H), 7.66 (d, *J* = 7.2 Hz, 2H), 7.79 (t, *J* = 7.2 Hz, 1H), 8.02 (d, *J* = 8.0 Hz, 1H);^{13}C NMR (400 MHz, $CDCl_3$): δ 14.4, 24.4, 26.9, 34.1, 61.2, 110.0, 124.9, 125.9, 126.6, 127.1, 128.1, 128.4, 128.5, 128.7, 129.5, 129.6, 130.1, 134.3, 134.4, 137.2, 139.5, 145.6, 147.0, 149.8, 150.1, 160.7, 161.5; EI-MS: m/z 488.26.

4-(4-Chloro-phenyl)-2-ethoxy-12-methyl-5,6-dihydro-benzo[*j*][1,7] phenanthroline-3-carbonitrile (4d):

Pale yellow solid; Yield 72 %; mp: 230-232 ˚C; FT-IR (KBr pellet) ν_{max}/ ($cm^{-}1$): 2225(CN), 1549, 1493 (C-O-C); ^1H NMR (400 MHz, $CDCl_3$) δ 1.52 (t, *J* = 8 Hz, 3H), 2.76 (t, *J* = 6.8 Hz 2H), 3.09 (t, *J* = 6.4 Hz, 2H), 3.15 (s, 3H), 4.57-4.63 (m, 2H), 7.33 (d, *J* = 8 Hz, 2H), 7.53 (d, *J* = 8 Hz, 2H), 7.59 (t, *J* = 7.6 Hz, 1H), 7.74 (t, *J* = 7.2 Hz, 1H), 8.02 (d, *J* = 8.4 Hz, 1H), 8.20 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (400 MHz, $CDCl_3$): δ 14.6, 17.3, 24.6, 33.5, 63.5, 94.5, 115.1, 124.9, 125.8, 126.0, 126.3, 128.6, 129.1, 129.2, 130.1, 130.3, 133.5, 135.7, 144.7, 147.1, 153.4, 155.1, 159.9, 162.1; EI-MS: m/z 426.27.

10-chloro-4-(3,4-dimethoxyphenyl)-2-ethoxy-12-phenyl-5,6-dihydrobenzo[*j*][1,7] phenanthroline (5a):

White solid; Yield 81 %; mp: 142-144 ˚C; : FT-IR (KBr pellet) ν_{max}/(cm^{-1}): 1552, 1477 (C-O-C); ^1H NMR (400 MHz, $CDCl_3$): δ 1.12 (t, *J* = 6.8 Hz, 3H), 2.88-2.90 (m, 2H), 3.16-3.17 (m, 2H), 3.32-3.34 (m, 2H), 3.91 (s, 3H), 3.95 (s, 3H), 6.86 (s, 1H), 6.94 (d, *J* = 8 Hz, 1H), 7.00 (d, *J* = 8 Hz, 1H), 7.24 (d, *J* = 6 Hz, 1H), 7.44-7.51 (m, 6H), 7.63 (d, *J* = 8.8 Hz, 1H), 7.99 (d, *J* = 8.8 Hz, 1H); ^{13}C NMR (100 Hz, $CDCl_3$): δ 14.3, 24.6, 33.8, 56.1, 56.2, 62.9, 95.3, 111.3, 112.1, 115.5, 121.8, 125.7, 126.0, 126.1, 127.3, 127.5, 128.6, 129.1, 129.5, 130.4, 131.2, 132.3, 138.3, 146.1, 146.4, 149.1, 150.1, 153.1, 154.8, 160.8, 162.0; ESI-MS: m/z 523.02.

10-chloro-4-(4-chlorophenyl)-2-ethoxy-12-phenyl-5,6-dihydrobenzo[*j*][1,7]phenanthroline (5b):

Yellow solid; Yield 79 %; mp: 236-238 ˚C; FT-IR (KBr pellet) ν_{max}/(cm^{-1}): 1544, 1492 (C-O-C); ^1H NMR (400 MHz, $CDCl_3$): δ 1.07 (t, *J* = 7.2 Hz, 3H), 2.92 (t, *J* = 7.2 Hz, 2H,), 3.15-3.28 (m, 4H), 6.46 (s, 1H), 7.38-7.47 (m, 8H), 7.58-7.60 (m, 2H), 7.98 (d, *J* = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.3, 24.3, 34.0, 61.2, 110.3, 125.0, 125.8, 126.6, 126.9, 128.3, 128.7, 129.2, 129.5, 130.1, 130.2, 131.8, 134.3, 137.0, 138.8, 144.6, 145.3, 149.3, 150.0, 161.1, 161.2; ESI-MS: m/z 497.26.

4-(4-Chloro-phenyl)-2-ethoxy-12-phenyl-5,6-dihydro-benzo[*j*][1,7]phenanthroline (5c):

Yellow solid; Yield 80 %; mp: 163-165 ˚C; FT-IR (KBr pellet) ν_{max}/ ($cm^{-}1$): 1545, 1493 (C-O-C); ^1H NMR (400 MHz, $CDCl_3$) δ 1.01-0.99 (t, *J* = 7.2 Hz ,3H), 2.90-2.87 (t, *J* = 7.6 Hz, 2H), 3.11 (t, *J* = 5.6 Hz, 2H), 3.24-3.19 (m, 2H), 6.52 (s, 1H), 7.27 (d, *J* = 7.2 Hz , 2H), 7.51-7.38 (m, 7H), 7.56 (d, *J* = 8.4 Hz, 2H), 7.78 (t, *J* = 7.6 Hz, 1H), 8.00 (d, *J* = 7.6 Hz, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ14.2, 24.4, 33.6, 62.9, 94.6, 115.1, 124.5, 125.4, 126.4, 127.1, 127.4, 128.1, 128.3, 128.6, 129.2, 129.5, 130.1, 130.4, 133.4, 135.7, 138.8, 147.5, 147.5, 147.6, 153.4, 153.8, 160.1, 161.9. ESI-MS: m/z 463.37.

4-(4-Chloro-phenyl)-2-ethoxy-12-methyl-5,6-dihydro-benzo[*j*][1,7]phenanthroline (5d):

Yellow solid; Yield 76 %; mp: 195-197 °C; FT-IR (KBr pellet) ν_{max}/(cm^{-1}): 1545, 1495 (C-O-C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.45 (t, *J* = 7.2 Hz, 3H), 2.87 (t, *J* = 7.2 Hz, 2H), 3.09 (t, *J* = 6.0 Hz, 2H), 3.16 (s, 3H) 4.50-4.45 (m, 2H,), 6.65 (s, 1H), 7.3 (d, *J* = 8.4 Hz, 2H), 7.45 (d, *J* = 8.0 Hz, 2H) 7.55 (t, *J* = 7.6 Hz, 1H), 7.70-7.67 (t, *J* = 7.2 Hz, 1H), 8.01 (d, *J* = 8.4 Hz, 1H), 8.18 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ13.8, 16.0, 23.6, 33.0, 60.8, 108.6, 123.6, 124.4, 124.8, 126.0, 127.7, 127.8, 127.9, 128.3, 129.1, 133.3, 136.2, 141.7, 145.5, 149.1, 150.2, 159.5, 160.3; ESI-MS: m/z 401.36.

10-chloro-4-(2-chlorophenyl)-2-ethoxy-12-phenyl-5,6-dihydrobenzo[*j*][1,7]phenanthroline (5e):

White solid; Yield 75 %; mp: 160-162 °C; FT-IR (KBr pellet) ν_{max}/(cm^{-1}): 1546, 1481 (C-O-C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.08 (t, *J* = 7.2 Hz, 3H,), 2.60-2.67 (m, 2H,), 2.78-2.85 (m, 2H), 3.17-3.26 (m, 2H), 6.41 (s, 1H), 7.34-7.36 (m, 2H), 7.40-7.50 (m, 8H), 7.58 (d, *J* = 8.8 Hz, 1H), 7.97 (d, *J* = 8.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.5, 23.9, 34.0, 61.3, 110.9, 125.9, 126.2, 126.7, 127.0, 128.4, 128.5, 129.4, 129.5, 129.6, 130.2, 130.3, 130.6, 131.8, 132.9, 137.7, 139.1, 144.7, 145.4, 148.8, 161.2, 161.4; ESI-MS: m/z 497.46.

10-chloro-4-(2,5-dimethoxyphenyl)-2-ethoxy-12-phenyl-5,6-dihydrobenzo[*j*][1,7] phenanthroline (5f):

White solid; Yield 78 %; mp: 138-140 °C; : FT-IR (KBr pellet) ν_{max}/(cm^{-1}): 1552, 1477 (C-O-C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.11-1.14 (t, *J* = 6.0 Hz, 3H), 2.88-2.90 (m, 2H), 3.17-3.18 (m, 2H), 3.33-3.34 (m, 2H), 3.91 (s, 3H), 3.95 (s, 3H), 6.86 (s, 1H), 6.94 (d, *J* = 8 Hz, 1H), 7.00 (d, *J* = 8.4 Hz, 1H), 7.26 (d, *J* = 8 Hz, 1H), 7.44-7.51 (m, 6H), 7.63 (d, *J* = 8.8 Hz, 1H), 7.99 (d, *J* = 8.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.3, 24.6, 33.8, 56.1, 56.2, 62.9, 95.3, 111.3, 112.1, 115.5, 121.8, 125.7, 126.0, 126.1, 127.3, 127.5, 128.6, 129.1, 129.5, 130.4, 131.2, 132.3, 138.3, 146.1, 146.4, 149.1, 150.1, 153.1, 154.8, 160.8, 162.0; ESI-MS: m/z 522.23.

10-chloro-2-ethoxy-4-(3-methoxyphenyl)-12-phenyl-5,6-dihydrobenzo[*j*][1,7] phenanthroline (5g):

Yellow solid; Yield 75 %; mp: 146-148 °C; : FT-IR (KBr pellet) ν_{max}/(cm^{-1}): 1558, 1543, 1442 (C-O-C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.06-1.09 (t, *J* = 6.8 Hz, 3H), 2.94 (t, *J* = 6.8 Hz, 2H), 3.16 (t, *J* = 6.0 Hz, 2H), 3.22-3.28 (m, 2H), 3.84 (s, 3H), 6.50 (s, 1H), 6.87 (s, 1H), 6.93 (t, *J* = 8.4 Hz, 2H), 7.25-7.29 (m, 2H), 7.34-7.41 (m, 2H), 7.44-7.46 (m, 3H), 7.58 (d, *J* = 8.8 Hz, 1H), 7.98 (d, *J* = 9.2 Hz, 1H): ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.5, 24.5, 34.3, 55.4, 61.3, 110.5, 113.7, 114.5, 121.3, 125.5, 125.9, 126.9, 127.0, 128.4, 129.4, 129.6, 129.7, 130.2, 130.3, 131.8, 139.0, 140.1, 144.7, 145.5, 149.3, 151.3, 159.7, 161.3, 161.4; ESI-MS: m/z 493.40.

10-chloro-2-ethoxy-4, 12-diphenyl-5,6-dihydrobenzo [*j*] [1,7]phenanthroline (5h):

Brown solid; Yield 75 %; mp: 150-152 °C: FT-IR (KBr pellet) ν_{max}/(cm^{-1}): 1552, 1477 (C-O-C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.13 (t, *J* =6.8 Hz, 3H), 2.81-2.84 (t, *J* =6.4 Hz, 2H), 3.17 (t, *J* =5.6 Hz, 2H), 3.31-3.36 (m, 2H), 7.15-7.36 (m, 4H), 7.44-7.50 (m, 8H), 7.63 (d, *J* = 8.8 Hz, 1H), 7.99 (d, *J* = 8.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.3, 24.4, 33.7, 62.9, 95.3, 115.2, 124.5, 124.5, 125.5, 125.8, 126.1, 126.8, 127.5, 128.0, 128.4, 128.6, 128.7, 128.9, 129.1, 129.4, 129.5, 130.2, 130.3, 131.2, 132.3, 132.5, 132.6, 135.1, 136.9, 138.3, 146.0, 146.4, 147.1, 153.1, 155.0, 160.8, 161.9; ESI-MS: m/z 462.29.

2-amino-10-choloro-5,6-dihydro-4-(3,4-dimethoxyphenyl)-12-pheny-4*H*-pyrano[2,3-*a*] acridine-3-carbonitrile (8a):

White solid; Yield 90%; mp: 206-208 °C; FT-IR (KBr pellet) ν_{max}/(cm^{-1}): 2372, 2193 (CN), 3448 (NH_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.07-2.11 (m, 1H), 2.38-2.42 (m, 1H), 2.97-2.91 (m, 1H), 3.07-3.10 (m, 1H), 3.7 (s, 6H,) 4.0 (s, 1H, CH), 4.9 (bs, 2H), 6.70-8.00 (m, 11H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 23.57, 32.15, 42.10, 55.42, 55.37, 111.17, 111.95, 118.37, 119.65, 119.81, 120.74, 124.45, 127.68, 127.88, 128.03, 128.18, 128.55, 128.73, 129.74, 130.54, 130.87, 135.72, 137.47, 139.56, 139.78, 144.29, 148.02, 148.84, 158.03, 158.98; ESI-MS: m/z 522.23.

2-amino-10-choloro-4-(4-chlorophenyl)-5,6-dihydro-12-pheny-4*H*-pyrano[2,3-*a*]acridine -3-carbonitrile (8b):

Yellow solid; Yield 82%; mp: 154-156 °C; FT-IR (KBr pellet) ν_{max}/(cm^{-1}): 2372, 2191 (CN), 3446 (NH_2); ^{1}H NMR (400 MHz, CDCl3): δ 2.15-2.20 (m, 1H), 2.39-2.41 (m, 1H), 2.99-3.06 (m, 1H), 3.12-3.16 (m, 1H), 4.0 (s, 1H), 3.4 (bs, 2H), 7.17-7.95 (m,12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 24.04, 32.82, 42.75, 59.73, 117.26, 119.22, 120.53, 125.57, 127.72, 128.14, 128.32, 128.56, 129.07, 129.20, 129.32, 129.42, 130.33, 130.60, 132.51, 133.75, 138.70, 140.64, 141.08, 141.18, 145.13, 158.22, 158.39; ESI-MS: m/z 495.35.

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† Electronic Supplementary Information (ESI) available.

CCDC 988643 contains 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 or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033; or e-mail: deposit@ccdc.cam.ac.uk.

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Graphical Abstract