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Palladium-Catalyzed Synthesis of 6*H*-Dibenzo[*c,h*]chromenes and 5,6-Dihydrobenzo[*c*]phenanthridines: Application to the Synthesis of Dibenzo[*c,h*]chromene-6-ones, Benzo[*c*]phenanthridines, and *Arnottin I*

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Abstract: 6*H*-Dibenzo[*c,h*]chromenes and 5,6-dihydrobenzo[*c*]phenanthridines have been synthesized via Palladium (II)-catalyzed domino reactions of acetylenic substrates involving intramolecular *trans*-oxo/amino palladation onto the triple bond followed by nucleophilic addition of the intermediate to a tethered cyano/aldehyde. The scope of this reaction was extended through one step conversion of some of the products to 6*H*-dibenzo[*c,h*]chromen-6-ones and benzo[*c*]phenanthridines. Utilization of this methodology led to a formal total synthesis of the natural product *Arnottin I.*

Keywords: Domino reaction; Palladium catalyst; 6*H*-Dibenzo[*c,h*]chromenes; 5,6-Dihydrobenzo[*c*]phenanthridines; *Arnottin I.*

1. Introduction

Fused heterocycles are of great importance because of their broad applications in different areas.[1] Among these compounds, the 6*H*-benzo[*c*]chromenes (**1 a**, Figure 1) are considered as privileged scaffolds and important substructures in modern drug discovery.[2] The related 6*H*-dibenzo[*c,h*]chromenes **2** also find extensive use as key synthetic intermediates of medicinally active compounds, besides offering easy access to dibenzo[*c,h*]chromen-6-ones **3** which constitute the core structures of a broad spectrum of natural products and others compounds possessing bactericidal properties.[3–8] These include *arnottin I*[3] (**5**, a non-alkaloidal minor component of *Xanthoxylum arnottianum*), *defucogilvocarcins* (**6 a**–**b**)[4] exhibiting antimicrobial activity, and *gilvocarcins* (**7 a**–**b**),[5] *ravidomycin* (**7 c**),[6] and *chrysomycins* (**7 d**–**e**)[7] belonging to the class of aryl C-glycoside antibiotics.[8]

Despite the promising biological effects[9] of 6*H*-dibenzo[*c,h*]chromenes **2**, this class of compounds is less explored compared to **3** in drug discovery primarily due to the lack of straightforward and convenient synthetic methods. Scrutiny of the literature revealed a single method[3h] for a general synthesis employing an intramolecular biaryl coupling reaction, while few other reports[10] deal with the preparation specific molecules during the course of the synthesis of either **1 a** or related compounds. This clearly pointed to the urgency of establishing a general and straightforward method for the synthesis of **2** starting from simple and easily accessible materials.

On the other hand, the aza-counterpart of **1 a** and its related structures such as dihydrophenanthridines (**1 b**, Figure 1), phenanthridinones (**1 c**, Figure 1) and phenanthridines are encountered in various alkaloids and synthetic compounds and display a wide range of pharmacological effects.[11] More importantly, fusion of an additional benzene ring to phenanthridines and their dihydro derivatives resulting in benzo[*c*]phenanthridines and its 5,6-dihydro derivatives (**4**) lead to products with remarkable therapeutic efficacies. For

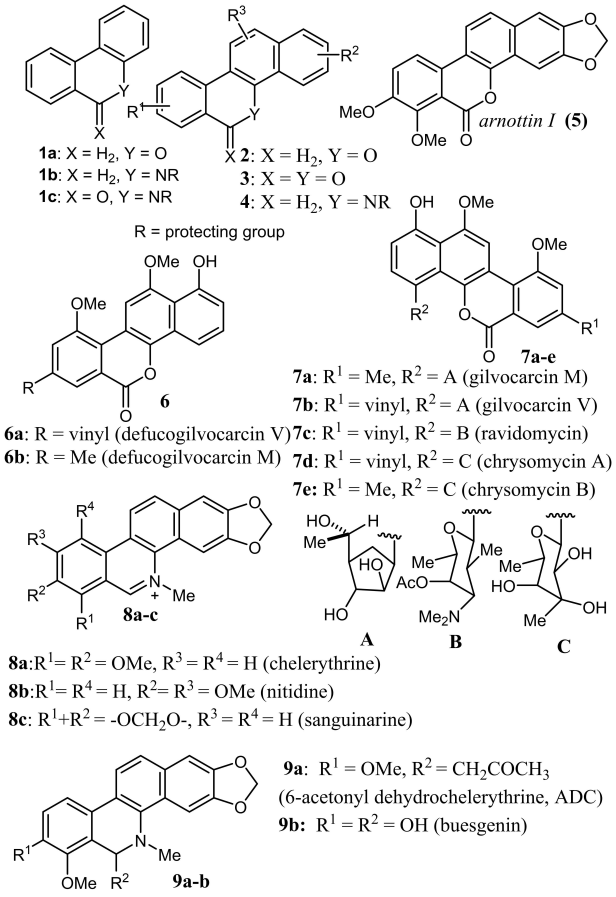


Figure 1. Biologically active dibenzo[*c,h*]chromen-6-ones 5–7, benzo[*c*]phenanthridines 8 and 5,6-dihydro- benzo[*c*]phenanthridines 9.

example, benzo[*c*]phenanthridine alkaloids **8a-c** (Figure 1) are reported to be G-quadruplex DNA stabilizer,[12a] topoisomerase I/II inhibitor,[12b] and lipoxygenase inhibitor,[12c] respectively. The 5,6-dihydro derivatives **4** are less naturally abundant but often exhibit distinct biological profiles. Thus *6-acetonyl dihydrochelerythrine* (ADC) **9a** (Figure 1) displays significant anti-HIV[13a] and anti-apoptotic[13b] effects, while *buesgenin* **9b**[13c] isolated from *Fagara tessmannii* exhibited high anti-bacterial activity while being non-toxic towards the normal cells. In spite of these encouraging results, there is no general method for the synthesis of **4** to date though few specific examples were reported[14] during the synthesis of other heterocycles. This underlined the urgency for the development of a facile and general method for the synthesis of **4**.

In recent times, domino reactions have emerged as efficient tools for the construction of complex molecules from the viewpoints of operational simplicity, atom economy and assemble efficiency.[15] In particular, reactions[16] involving 1,2-addition of a vinyl palladium species onto a carbon-heteroatom multiple bond (e.g., –CO–, –CHO, –CN) followed by protonation of the resulting intermediate have proved to be useful in the field of heterocycle synthesis after the seminal works of Larock,[16a] Lu[16b] and Wang.[16c] In continuation of our work on palladium-catalyzed reactions,[17] we therefore anticipated that a general synthesis of 6*H*-dibenzo[*c,h*]chromenes **2** and 5,6-dihydrobenzo[*c*]phenanthridines **4** could be achieved in atom economical way through one-pot domino reactions using readily available substrates. Our concept proved to be viable upon choosing appropriate reaction conditions and catalyst. The results obtained so far are described herein.

2. Results and Discussion

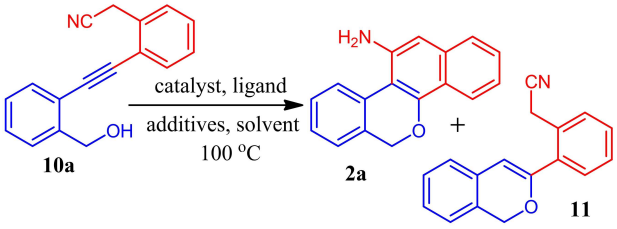
2.1. Synthesis of 6*H*-dibenzo[*c,h*]chromene derivatives 2/2′

We commenced the investigation with a model study on substrate **10a** which can be easily accessed through *Sonogashira coupling* between *o*-ethynylbenzyl alcohol and *o*-iodobenzyl cyanide (see Scheme S1 under supporting information); selected results are presented in Table 1. Notably, $Pd(OAc)_2$ or its ligated complex [i.e., $Pd(OAc)_2$bpy] turned out to be superior to other palladium catalysts (results not shown). Still, employment of 5 mol% of $Pd(OAc)_2$bpy in 1,4-dioxane furnished the desired product **2a** to the extent of 38% only along with the side product **11** resulting from mono-cyclization (Table 1, entry 1). Even deployment of catalyst and ligand separately in dry THF did not quite improve the situation (Table 1, entry 2), so we decided to test polar solvents. Indeed, carrying out this reaction in DMA enhanced the yield of **2a** to 52% with complete suppression of the side product **11**, though the relatively less polar DMF did not prove to be so efficient (Table 1, entries 3 & 4). Pleasingly, replacement of DMA by a still more polar solvent (NMA) significantly improved the yield (75%) of **2a** and reduced the reaction time from 6 h to 2 h (Table 1, entry 5). But the use of $Pd(OAc)_2$bpy or $Pd(OAc)_2$phen reduced the yield of **2a** marginally (Table 1, entry 6,7) and required longer reaction periods (Table 1, entry 7).

In order to optimize the reaction conditions further, we then replaced D-CSA with *p*-toluenesulphonic acid (*p*-TsOH); to our dismay, a mixture of the desired product **2a** and side product **11** (~1:1) resulted[18] (Table 1, entry 8), establishing the superiority of D-CSA.

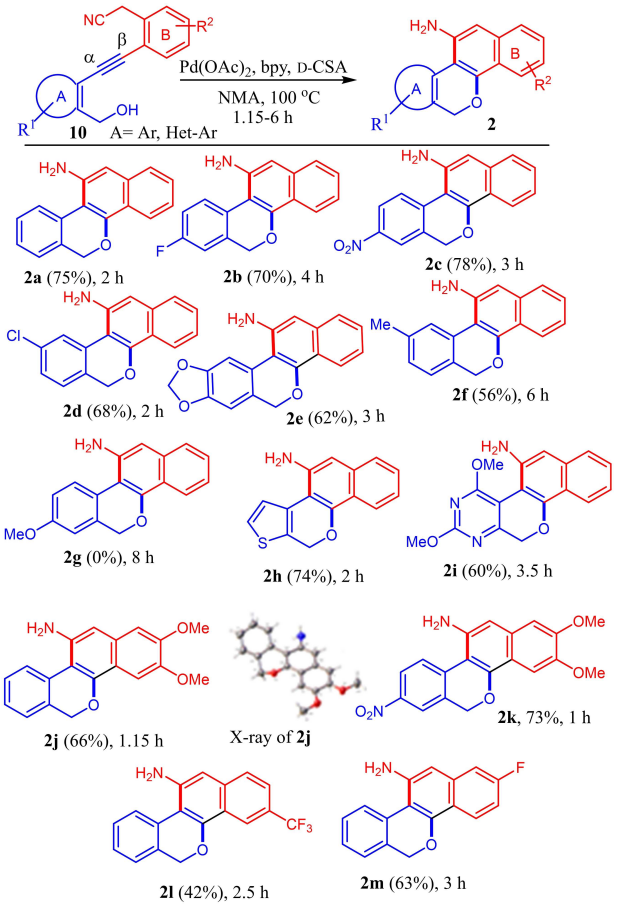
On the other hand, removal of D-CSA from the reaction did not produce **2a** at all, proving its necessity in this reaction (Table 1, entry 9), while carrying out this reaction using D-CSA alone was also unsuccessful (Table 1, entry 10). Thus reaction conditions of entry 5 of Table 1 appeared to be optimal.

Table 1. Optimization of the reaction conditions for 6*H*-dibenzo[*c*,*h*]chromen-11-amine **2a**.[a]



Entry	Catalyst	Additives	Solvents	Time	Yield[b] 2a	11
1	$Pd(OAc)_2$bpy	D-CSA	1,4-dioxane	4	38	20
2[c]	$Pd(OAc)_2$	D-CSA	THF	6	40	25
3[c]	$Pd(OAc)_2$	D-CSA	DMF	8	20	
4[c]	$Pd(OAc)_2$	D-CSA	DMA	6	52	
5[c]	**$Pd(OAc)_2$**	**D-CSA**	**NMA**	**2**	**75**	
6	$Pd(OAc)_2$bpy	D-CSA	NMA	2	72	
7	$Pd(OAc)_2$phen	D-CSA	NMA	3	68	
8[c]	$Pd(OAc)_2$	*p*-TsOH	NMA	2	45	50
9[c,d]	$Pd(OAc)_2$	-	NMA	20	nr	
10[d]	-	D-CSA	NMA	8	nr	

[a] Reaction conditions: **10a** (0.2 mmol), catalyst (5 mol%, except entry 10), bpy (6 mol%, except entries 1, 6–7 and 10), and additive (1.5 equiv.) in solvent (2 mL) at 100 °C under argon atmosphere.
[b] Isolated pure products.
[c] Ligand bpy (6 mol%) was used.
[d] The starting compound **10a** was found to remain intact (TLC).
Abbreviations: bpy: bipyridine; phen: phenanthroline; D-CSA: D-(+)-camphor sulfonic acid; NMA: N-methylacetamide; n.r.: no reaction.



[a] Reaction conditions: **10** (0.20 mmol), Pd(OAc)2 (5 mol %, bpy (6 mol %) and D-CSA (1.5 equiv.) in NMA (2 mL) under argon atmosphere.
[b] Yield of the isolated pure product.

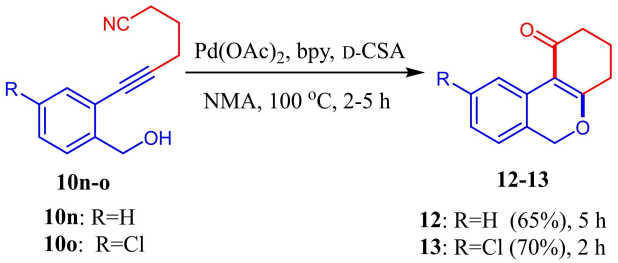
Scheme 1. Palladium-catalyzed synthesis of 11-amino-6*H*-dibenzo[*c*,*h*]chromenes **2**.[a,b]

We next set out to explore the scope and generality of the reaction on a variety of substrates **10** as shown in Scheme 1. A series of products **2a–l** could easily be prepared within 1.2–6 h with moderate to very good yields (42–78%) and a range of functional groups (viz., Me, CF_3, OMe, F, Cl, NO_2, CO_2Me, NH_2) were tolerated. An electron withdrawing group (EWG) in phenyl ring A facilitated the reaction, affording the desired products **2b–d** within 3–4 h with very good yields (68–78%). In contrast, an electron donating group at *meta* position (viz., R^1 = Me) made the reaction somewhat sluggish with lower yield (56%) of the product (**2f**), though the presence of two EDGs at *meta* and *para* positions (viz., R^1 = –OCH_2O–) delivered the product **2e** within 3 h. Notably, placement of a strong electron donating group (viz., OMe) at *para* position did not furnish any desired product **2g** even after heating for 8 h; the starting material remained intact (TLC) instead. However, replacement of the aryl ring A of **10** by a heteroaryl one (thiophene/2,4-dimethoxypyrimidine) worked well, affording the product (viz., **2h**/**2i**) within 2–3.5 h with 60–74% yields.

Regarding the effect of substituents in the other phenyl ring (i.e., B) of **10**, introduction of electron donating methoxy groups both at *meta* and *para* positions reduced the reaction time (1.15 h) significantly and produced the expected product **2j** in good yield (66%). The reaction was facilitated further by the incorporation of an additional nitro group (EWG) in ring A *para* to the alkyne group, resulting in the formation of product **2k** (73%). On the other hand, an EWG (viz., R^2 = CF_3 or F) at either *meta* or *para* position of ring B lowered the yields of the desired products (**2l** or **2m**) even after prolonging the reaction time (2.5–3 h). These substituent effects are perhaps predictable keeping in view the importance of electro-

philicity of *β*-carbon (of the triple bond of **10**) for the cyclization to proceed smoothly.

We also noted that performing this reaction with substrates having the acetylenic carbon tethered to a cyano group through a C3 chain (**10n–o**) instead of a benzylic moiety resulted in carbonylated products **12–13** within 2–5 h with 65–70% yield (Scheme 2) which is in line with previous observations. [19]



10n-o **12-13**

10n: R=H
10o: R=Cl

12: R=H (65%), 5 h
13: R=Cl (70%), 2 h

Scheme 2. Synthesis of 2,3,4,6-tetrahydro-1*H*-benzo[*c*]chromen-1-ones **12–13**.

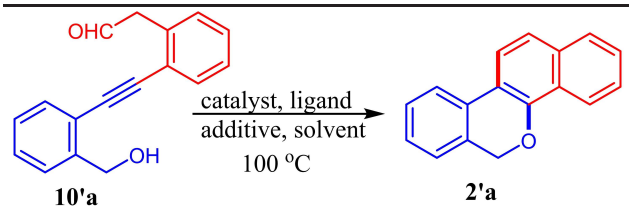
2.2. Synthesis of 6*H*-dibenzo[*c,h*]chromenes 2′

Encouraged by these results, we became interested to apply the reaction on other substrates **10′** in which an aldehyde functionality is used in place of a cyano group. To our dismay, this reaction produced **2′a** with only 42% yield (Table 2, entry 1). But use of the less polar 1,4-dioxane instead of NMA proved beneficial, delivering the expected product within 2 h with 75% yield (Table 2, entry 2). Though removal of the additive or changing the ligand to phenanthroline did not help (Table 2, entries 3 and 4), use of a ligated catalyst [i.e., $Pd(OAc)_2$bpy instead of $Pd(OAc)_2$ and bpy separately] greatly improved the yield (Table 2, entry 5). Replacing D-CSA by *p*-TsOH or decreasing the polarity of the solvent further had detrimental effect on the yield (Table 2, entries 6–8). Thus the reaction conditions of entry 5 of Table 2 appeared best.

To establish the generality of this methodology, the optimized reaction condition was then applied to a range of substrates (Scheme 3). Various substituents (e.g. NO_2, OMe, Me, F, Cl, Br etc.) in the aryl moiety of substrate **10′** were well tolerated. But a strongly electron-withdrawing group ($R^1 = NO_2$) in ring A *para* to the alkyne moiety lowered the yield of the product (**2′b**, 56%) considerably, while moderately active ones (R^1 = F/Cl/Br) either at *para* or *meta* position had little impact (**2′c**/**2′d**/**2′e**). Of particular note, employment of an electro-donating group (viz., R^1 = OMe) at *para* position in the same ring (**10′f**) yielded no product, leaving the starting material intact (TLC); this result is in line with our previous observation (see, product **2g** in Scheme 1). The inertness of these substrates (**10g**/**10′f**) is perhaps attributable to the enhanced electron density on the β-carbon of the triple bond, involved in the intramolecular nucleophilic attack, by the hydroxy methylgroup [see, species **A** (Y=O) under Scheme 10, *vide infra*]. In contrast, when the methoxy groups are placed at meta and para positions in ring B of the substrate (**10′g**), the expected product **2′g** was indeed formed smoothly with very good yield (75%); the high reactivity of this substrate is likely due to the electron-donating effect of the methoxy group making the same carbon atom (*β*) of the triple bond electron deficient, thereby facilitating the cyclization through the nucleophilic hydroxyl group.

As anticipated, employing an electron-withdrawing substituent (viz., R^2 = F) at *para* position (substrate **10′h**) indeed produced the product **2′h**, though in reduced yield (62%) as compared to **2′c**. On the other hand, the use of an electron donating methyl group at *meta* position (**10′i**) led to the product **2′i** with a moderate yield (47%). Even the substrate **10′j** with an alpha substituted aldehyde group reacted equally well, showing no influence of the steric effect at this site.

Table 2. Optimization of the reaction conditions for 6*H*-dibenzo[*c,h*]chromene **2′a**.[a]



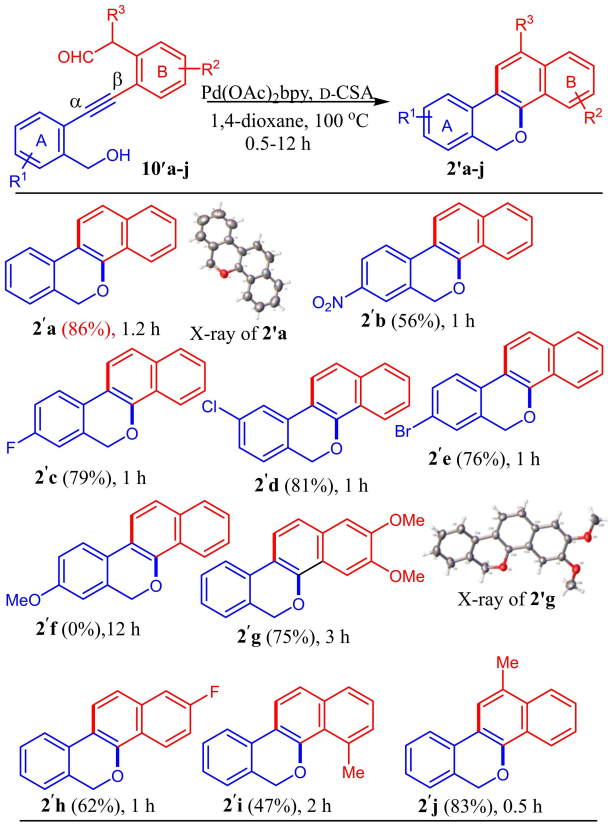
10'a **2'a**

Entry	Catalyst	Ligand	Additives	Solvent	Time (h)	Yield (%)[b]
1	$Pd(OAc)_2$	bpy	D-CSA	NMA	2.5	42
2	$Pd(OAc)_2$	bpy	D-CSA	1,4 dioxane	2	75
3[c]	$Pd(OAc)_2$	bpy	-	1,4 dioxane	48	n.r.
4	$Pd(OAc)_2$	phen	D-CSA	1,4 dioxane	2	58
5	**$Pd(OAc)_2$(bpy)**	-	**D-CSA**	**1,4 dioxane**	**1.6**	**86**
6	$Pd(OAc)_2$(bpy)	-	p-TsOH	1,4 dioxane	1	80
7	$Pd(OAc)_2$(bpy)	-	D-CSA	THF	1.5	61
8	$Pd(OAc)_2$	bpy	D-CSA	THF	2.5	62

[a] Reaction conditions: **10′a** (0.2 mmol), catalyst (5 mol%,), ligand (6 mol%), and additive (1.5 equiv.) in solvent (2 mL) at 100 °C under argon atmosphere.
[b] Isolated pure products.
[c] Starting material was recovered. Abbreviations: n.r.: no reaction, bpy: bipyridine, phen: phenanthroline.

2.3. Synthesis of dibenzo[*c,h*]chromen-6-ones 3

After achieving a general synthesis of 6*H*-dibenzo[*c,h*] chromenes **2**/**2'**, we became interested to test the

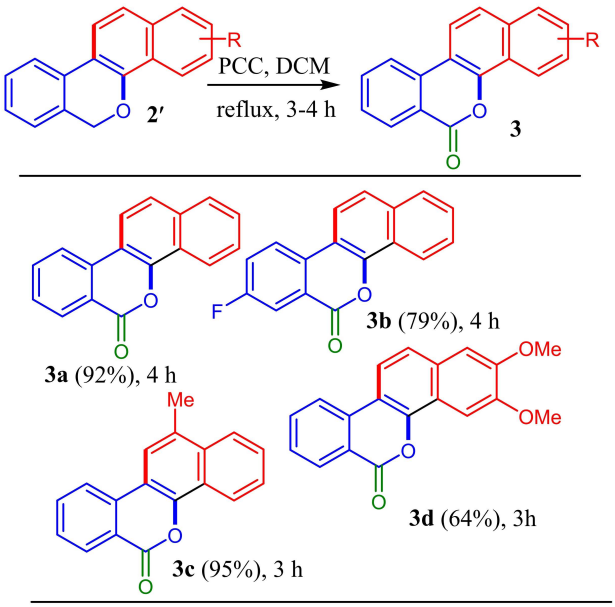


[a] Reaction conditions; **10′** (0.2 mmol), Pd(OAc)2bpy (5 mol %) and D-CSA (1.5 equiv. in 1,4-dioxane (2 mL) at 100 °C under argon atmosphere.
[b] Yield of the isolated pure products.

Scheme 3. Palladium-catalyzed synthesis of 6*H*-dibenzo[*c*,*h*] chromenes **2′**.[a,b]

applicability of this reaction through synthetic transformation of the products prepared. Initially we attempted benzylic oxidation of products **2′** which could provide easy access to **3**. Of the various oxidizing agents tested, PCC appeared to be the best, furnishing the desired products **3a–d** within few hours with very good to excellent yields (79–95%, Scheme 4). Thus synthesis of dibenzo[*c*,*h*]chromen-6-ones **3** could easily be achieved in two steps starting from acetylenic substrate **10** and overall yields were found to be between 48–81%.

In view of the prospect of synthesizing the products **3** directly, we carried out a reaction on substrate having *ortho*-carboxylic acid group in place of benzylic alcohol (of **10′a**) under our optimized reaction conditions (entry 5 of Table 2); to our surprise, the desired product **3a** was still found to be formed within 2 h but only in moderate yield (42%) (See, Scheme S4 under Supporting Information).



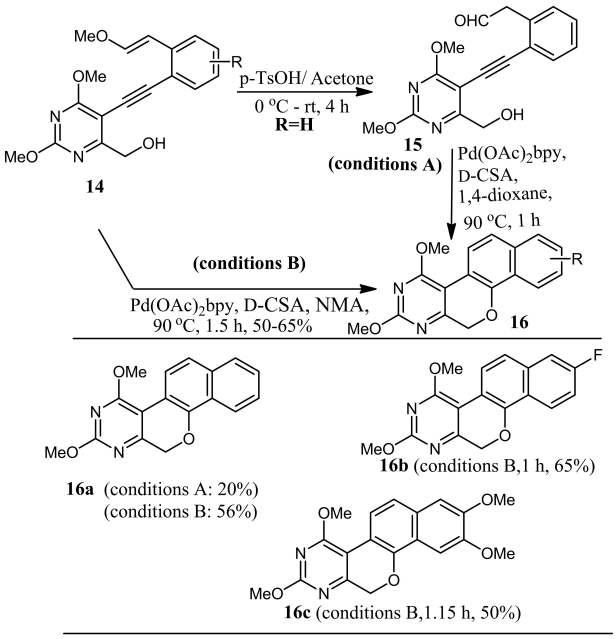
[a] Reaction conditons: A mixture of **2′** (0.086 mmol) and PCC (1.5 equiv.) in DCM (2 mL) was refluxed under argon atmosphere.
[b] Yield of the isolated pure product.

Scheme 4. Conversion of products **2′** to 6*H*-dibenzo[*c*,*h*]chromen-6-ones **3**.[a,b]

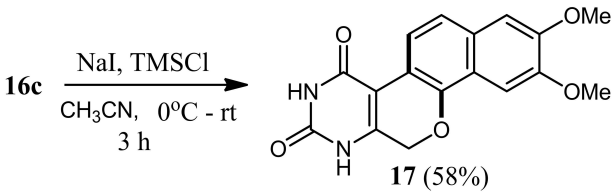
2.4. Synthesis of Pyrimidine (16) and Uracil (17) Derivatives

In view of the immense biological activity of uracil derivatives in cancer chemotherapy[20a–d] and our own interest in this field,[20e] we decided to apply the methodology for the synthesis of such molecules. The requisite starting material **15**, synthesized from precursor masked aldehyde **14a** (R=H) by treating with *p*-TsOH, was exposed to conditions A as shown in Scheme 5; to our disappointment, the desired product **16a** (R=H) was obtained only in 20% yield. Gratifyingly, the masked aldehyde **14a**, used under conditions B (where NMA is used instead of 1,4-dioxane), responded better and furnished the desired product **16a** with 56% yield. Substrates **14b** and **14c** containing electron withdrawing (R=F) and donating (R=OMe) group, respectively, also proved to be effective, affording the expected products (**16b** and **16c**) with 50–65% yield (Scheme 5).

For transformation to uracil derivatives, one of the products was tested for chemoselective demethylation. When **16c** was treated with TMSCl/NaI at room temperature (Scheme 6), the desired product **17** was formed easily albeit in moderate yield (58%). Anticancer screening of **17** in various cell lines and preparation of other related uracil derivatives are currently underway.



Scheme 5. Synthesis of 2,4-dimethoxy-12*H*-benzo[7,8]chromeno[3,4-*d*]pyrimidines **16**.



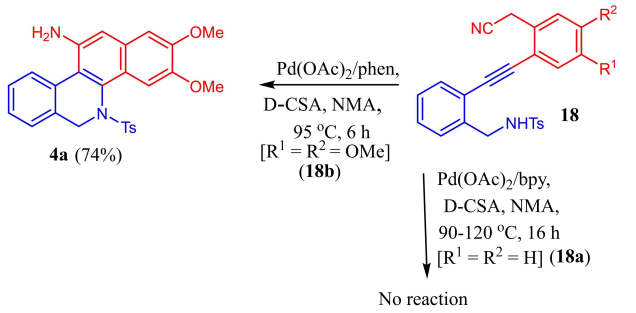
Scheme 6. Conversion of **16c** to uracil derivative **17**.

3. Synthesis of the Aza Analogues

3.1. Synthesis of N-tosyl-5,6-dihydrobenzo[c]phenanthridines 4/4′

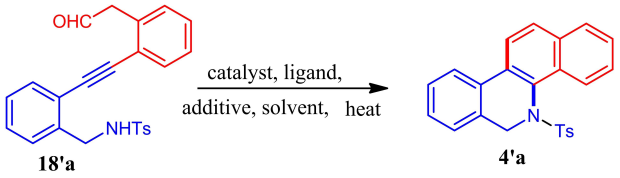
After successful exploration of the general synthesis of 6*H*-dibenzo[*c,h*]chromenes **2/2′**, we became interested to check the feasibility of this reaction for nitrogen heterocycles **4**. Initially, the starting material **18a** (R^1=R^2=H) was synthesized (see Scheme S5 under supporting information) and allowed to react under the optimized reaction conditions (entry 5 of Table 1). To our surprise, it merely yielded a tarry product (Scheme 7). The situation did not improve even after altering the catalyst, ligands, solvent systems, and temperature, or through incorporation of common substituents (R^1=Cl/F, R^2=H). Only when electron donating methoxy groups were incorporated in the substrate (R^1=R^2=OMe; **18b**), the desired product **4a** was formed.

We then planned to modify the structure of substrate **18** by replacing its cyano group with a formyl one. Towards this, the substrate **18′a** prepared in few steps (see Scheme S6 under supporting information) was subjected to the optimized reaction conditions (see entry 5 of Table 2), but the desired product **4′a** was formed with only 53% yield (Table 3, entry 1). Even the use of catalyst and ligand separately instead of preformed $Pd(OAc)_2$bpy was not helpful (Table 3, entry 2). But switching to a less polar solvent (i.e., THF) reduced the reaction time to 2 h and improved the yield to 62% (Table 3, entry 3). Use of the preformed catalyst $Pd(OAc)_2$bpy improved it further (Table 3, entry 4). But the reaction carried out in NMA required (Table 3, entries 5–6) longer time (2.5–3 h) and resulted in lower yields (38–41%), arguing against



Scheme 7. Palladium-catalyzed synthesis of 5,6-dihydrobenzo[*c*]phenanthridin-11-amines **4**.

Table 3. Optimization of the reaction conditions for *N*-tosyl-5,6-dihydrobenzo[*c*]phenanthridine **4′a**.[a,b]



Entry	Catalyst	Ligand	Solvent	Temp (°C)	Time (h)	Yield (%)[c]
1	$Pd(OAc)_2$bpy	-	1,4-dioxane	100	2	53
2	$Pd(OAc)_2$	bpy	1,4-dioxane	100	3	50
3	$Pd(OAc)_2$	bpy	THF	Reflux	2	62
4	**$Pd(OAc)_2$bpy**	-	**THF**	Reflux	**1.3**	**78**
5	$Pd(OAc)_2$bpy	-	NMA	100	2.5	41
6	$Pd(OAc)_2$phen	-	NMA	100	3	38

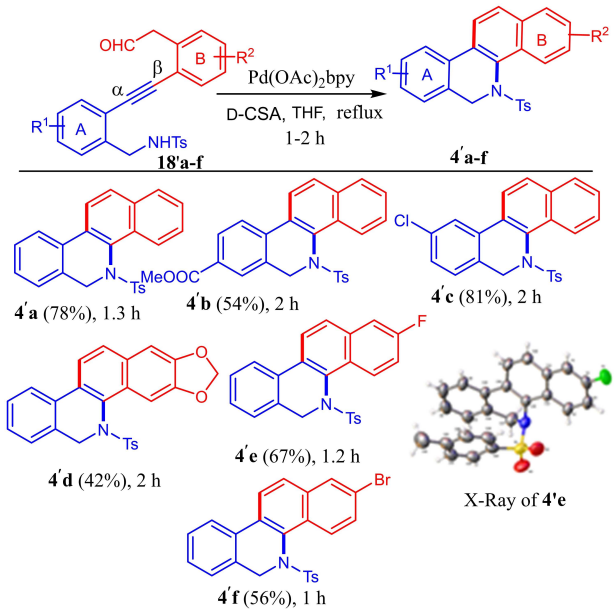
[a] In all entries, D-CSA was used as an additive.
[b] Reaction conditions: A mixture of **18′a** (0.2 mmol), catalyst (5 mol%), ligand (6 mol%), and D-CSA (1.5 equiv.) in solvent (2 mL) was heated at the mentioned temperature under argon atmosphere.
[c] Yield of the isolated pure products.

the use of polar solvent systems. Thus, the reaction conditions of entry 4 proved optimum.

To establish the generality of the synthesis of **4′**, we applied the optimized reaction conditions on substrates **18′** having various substitutions (Scheme 8). Initially, we used a strong electron-withdrawing group (viz., R^1=CO_2Me) in ring A *para* to the alkyne moiety of substrate **18′b**; indeed, it furnished the desired product **4′b** in 2 h with 54% yield, while a moderately electron-withdrawing group (i.e., R^1=Cl) at *meta* position afforded the desired product **4′c** with very good yield (81%). However, attempts to prepare a substrate containing an electron-donating methoxy group (R^1=OMe) in place of the carbomethoxy (of **18′b**) failed despite our sincere efforts.

Regarding the effect of ring B substituents, an electron-donating methylenedioxy group as in substrate **18′d** resulted in product **4′d** within 2 h albeit in moderate yield (42%). While the electron-withdrawing fluoro group at *para* position (**18′e**) afforded the product **4′e** in 1.2 h with a good yield (67%), the less electron-withdrawing bromo group (in **18′f**) lowered the reaction time (1 h) but also the yield (56%) simultaneously.

Addtionally, in order to check the role of N-protecting group in substrate **18′**, we deliberately replaced the tosyl group of the same by acetyl or Boc and the resulting substrates were allowed to react separately under optimized reaction conditions (entry 4 of Table 3); to our surprise, no trace of product formation (TLC) was observed in each case even after heating the reaction for several hours; the starting material was recovered instead.

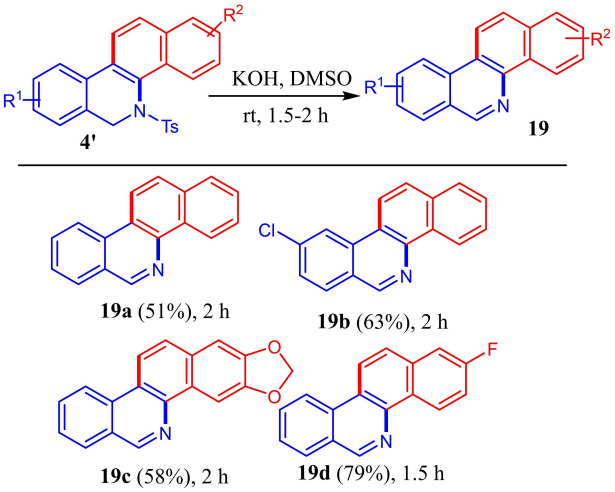


[a] Reactions conditons: **18′**(0.2 mmol), Pd(OAc)2bpy (5 mol %) and D-CSa (1.5 equiv.) in refluxing THF (2 mL) under argon atmosphere.
[b] Yield of the isolated pure products.

Scheme 8. Palladium-catalyzed synthesis of *N*-tosyl-5,6-dihydrobenzo[*c*]phenanthridines **4′**.[a,b]

3.2. Synthesis of Benzo[*c*]phenanthridines 19

Though some traditional[21a–d] and palladium-catalyzed methods[21e–g] for the synthesis of **19** exist in the literature, we felt that synthesis could easily be attained from **4′** through a base induced elimination reaction. Screening of a range of organic and inorganic bases proved potassium hydroxide to be the best for this transformation (Scheme 9). Thus the desired products were synthesized conveniently within 1.5–2 h with moderate to very good yields (51–79%) and the process was compatible with different functional groups (e.g., F, Cl and –OCH_2O–).

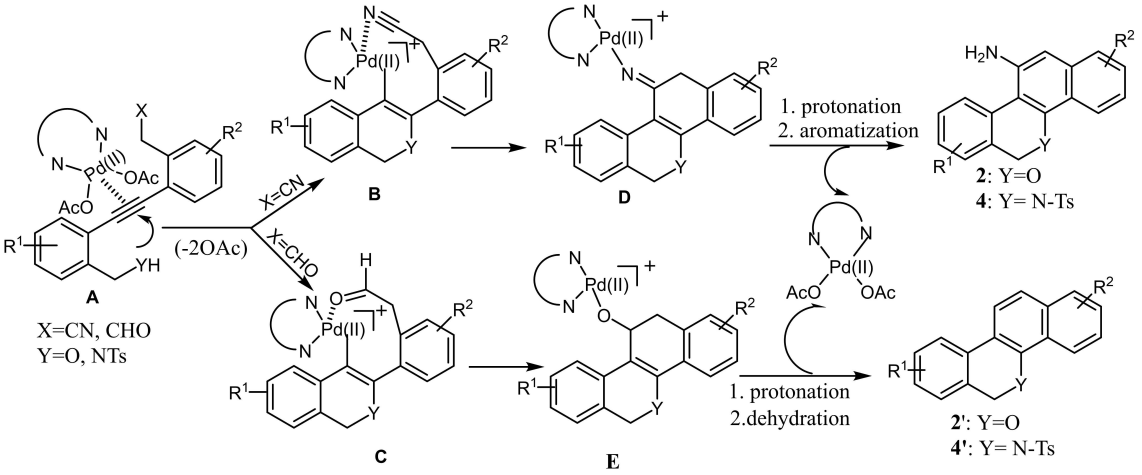


[a] Reaction condition: A mixture of **4′**(0.13 mmol) and KOH (5 equiv.) in DMSO was stirred at room temperature under argon atmosphere.
[b] Yield of the isolated product.

Scheme 9. Base promoted synthesis benzo[*c*]phenanthridines **19**.[a,b]

The structures of all products (i.e., **2/2′**, **3**, **4/4′**, **16–17, 19**) were established firmly by spectroscopic (^{1}H[22] and ^{13}C NMR, HRMS) and analytical data. In addition, single crystal X-ray analysis[23] of **2j** (Scheme 1), **2′a** and **2′g**, Scheme 3) and **4′e** (Scheme 8) provided additional support to the structural conclusion.

On the basis of our experimental results and known palladium chemistry, a plausible reaction mechanism is depicted (Scheme 10) to explain the product formation. Thus initial activation of the triple bond of the acetylenic substrate by the Pd(II) catalyst leads to the formation of species **A** which may trigger heteroannulation through *trans*-oxo/amino palladation

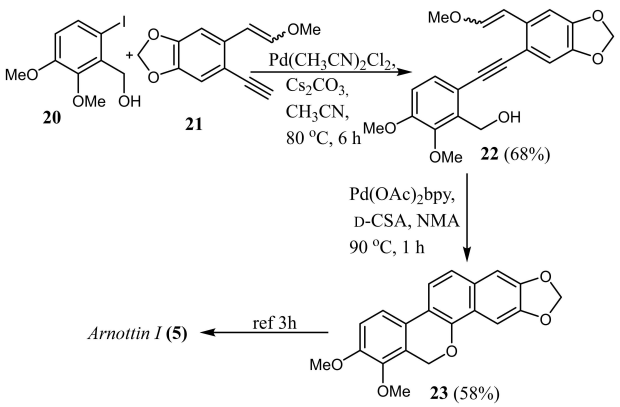


Scheme 10. Plausible mechanism for the formation of products **2/4** and **2′/4′**.

pathway[17e,24] resulting in the formation of the transient intermediate species **B** or **C**.[25] Next, species **B** and **C** may undergo intramolecular Grignard type nucleophilic addition over a tethered cyanide/aldehyde group to produce the corresponding palladated species **D**[16c] and **E**[26a–b], respectively. While species **D** upon protonolysis using D-CSA followed by aromatization would lead to the targeted product **2/4**, similar protonolysis on species **E**[27] followed by dehydration would afford the product **2′/4′**.

4. Application to the Formal Total Synthesis of *Arnottin I* (5)

In order to enlarge the scope of this heteroannulation reaction further, we undertook a total synthesis of *Arnottin I* (**5**, Figure 1) in a concise manner. This natural product was isolated as a minor constituent from the bark of *Xanthoxylum arnottianum,*[3a–b] but the biological activities have not been explored fully because of its low natural abundance. Nevertheless, related natural products have aroused significant interest in medicinal chemistry. For example, *neotanshinlactone* displayed potent activity against human breast cancer cell lines,[28] while *chelerythrine* (**8a** in Figure 1) proved to be of interest in cancer chemotherapy due to its ability to stabilize the c-MYC and c-KIT quadruplex DNAs[29a–b] (overexpression of which has been associated[29c] with numerous cancers) in addition to its role as G-quadruplex DNA stabilizer.[12a] These findings provided impetus to develop various strategies[3b–h] in order to get easy access to **5**. However, some of them use long synthetic routes using conventional reagents,[3b,f–g] while others, employing either palladium[3c–d,h] or nickel catalyst,[3e] required starting materials that were difficult to access. We felt that an intramolecular heteroannulation of intermediate **22**, which in turn could be synthesized through a palladium-catalyzed coupling between **20**[30] and **21**[14b] (see supporting information), may lead to **23** by adopting our newly developed method, the oxidation (PCC) of the benzylic hydrogens of which would provide easy access to *Arnottin I.* It is important to mention that the masked aldehyde precursor **22** should be preferred as substrate. Indeed, the desired product **23** was thus isolated in 58% yield within 1 h as shown in Scheme 11.



Scheme 11. Formal total synthesis of *Arnottin I* (**5**).

5. Conclusion

In conclusion, we have described a palladium-catalyzed expeditious approach for the general synthesis of dibenzo[*c,h*]chromen-6-ones **2/2′** and 5,6-dihydrobenzo[*c*]phenanthridines **4′** through intramolecular domino reactions of acetylenic substrates involving *trans*-oxo/aminopalladation followed by nucleophilic addition to

cyanide or aldehyde group. The method is fast, atom economical, operationally simple, and uses readily available substrates. A range of functional groups could easily be accommodated at different sites leaving enough opportunity for diversification. Simple one-step conversion of our products paved the way for easily accessing 6*H*-dibenzo[*c,h*]chromen-6-ones **3** and 5,6-dihydrobenzo[*c*]phenanthridines **19** prevalent as core structures of many medicinally active compounds. Finally, a concise formal total synthesis of *Arnottin I* was accomplished by applying the developed method. Thus we have successfully generated rapid molecular complexity under one pot using simple acetylenic substrates avoiding any by-product. We believe that this method will find applications in the total synthesis of complex natural products and medicinally relevant molecules as well.

Experimental Section

General Information

All solvents were distilled prior to use. Petroleum ether refers to fraction boiling in the range 60–80 °C. Dichloromethane was dried over phosphorous pentoxide, distilled, and stored over 3 Å molecular sieves in a sealed container. 1,4-Dioxane was distilled over sodium and benzophenone. Commercial grade dry DMF (Dimethylformamide), DMA (Dimethylacetamide), and NMA (*N*-Methylacetamide) were used as solvents. All reactions were carried out under argon atmosphere and anhydrous conditions unless otherwise noted. Analytical thin-layer chromatography (TLC) was performed on silica gel 60 F254 aluminum TLC sheets. Visualization of the developed chromatogram was performed by UV absorbance or iodine exposure. For purification, column chromatography was performed using 100–200 mesh silica gel. ^{1}H and ^{13}C NMR spectra were recorded on a 300, 400 or 600 MHz spectrometer using tetramethylsilane (TMS) as internal standard. Chemical shifts (δ) are given from TMS (δ = 0.00) in parts per million (ppm) with reference to the residual nuclei of the deuterated solvent used [$CDCl_3$: ^{1}H NMR δ = 7.26 ppm (s); ^{13}C NMR δ = 77.0 ppm]. Coupling constants (*J*) are expressed in Hertz (Hz), and spin multiplicities are given as s (singlet), d (doublet), dd (double doublet), t (triplet), td (triple doublet), q (quartet), m (multiplet), and br (broad). All ^{13}C NMR spectra were obtained with complete proton decoupling. Mass spectra were performed using ESI-TOF or EI mode.

General Procedure for the Synthesis of 6*H*-dibenzo [*c,h*]chromen-11-amine 2

A mixture of $Pd(OAc)_2$ (2.2 mg, 0.01 mmol, 5 mol%), 2,2′-bipyridine (1.9 mg, 0.012 mmol, 6 mol%) and D-CSA(69.6 mg, 0.3 mmol, 1.5 equiv.) in dry NMA (3 mL) was stirred at 90 °C for 5 min under argon atmosphere. Next, the starting material **10** (0.20 mmol) dissolved in NMA (1.5 mL) was added to the reaction mixture at the same temperature and the whole mixture was allowed to stir at heating conditions (100 °C) for few hours until the completion of the reaction (TLC). The reaction mixture was then neutralized by adjusting the pH (~7) through drop wise addition of 20% aqueous sodium bicarbonate solution and extracted with ethyl acetate (3 × 20 mL). The combined organic extracts were washed with saturated brine (10 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The resulting residue was purified through silica gel (100–200 mesh) column chromatography using 10–40% ethyl acetate-petroleum ether (v/v) as eluent to afford the desired product **2**.

6H-Dibenzo[c,h]chromen-11-amine (2a): Brown gum (37.2 mg, 75% yield), R_f = 0.41 (10% ethyl acetate in petroleum ether, v/v); ^{1}H NMR ($CDCl_3$, 300 MHz) δ_H 8.32 (d, *J* = 7.8 Hz, 1H), 8.11 (d, *J* = 8.4 Hz,1H), 7.54 (d, *J* = 8.1 Hz, 1H), 7.44-7.34 (m, 2H), 7.32 (d, *J* = 3.9 Hz, 2H), 7.24–7.19 (m, 1H), 6.78 (s, 1H), 5.12 (s, 2H), 4.20 (bs, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ_C 152.8, 141.9, 134.8, 132.3, 129.9, 128.5, 127.4, 127.0, 125.3, 125.2,123.6, 122.3, 122.2, 120.0, 110.7, 104.2, 69.4; HRMS (ESI+) m/z calculated for $C_{17}H_{14}NO$ $[M+H]^+$ 248.1075, found 248.1083.

8-Fluoro-6H-dibenzo[c,h]chromen-11-amine (2b)*:* Brown solid (37.1 mg, 70% yield), mp 120–122 °C, R_f = 0.41 (10% ethyl acetate in petroleum ether, v/v); ^{1}H NMR ($CDCl_3$, 300 MHz) δ_H 8.34–8.29 (m, 1H), 8.08 (d, *J* = 8.4 Hz, 1H),7.54 (d, *J* = 8.1 Hz, 1H), 7.38 (t, *J* = 7.8 Hz, 1H), 7.23–7.20 (m, 1H), 7.13–7.01 (m, 1H), 6.78 (s, 1H), 5.08 (s, 2H), 4.12 (bs, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ_C 161.6 (d, *J* = 246.6 Hz), 152.3, 141.7, 134.7, 134.6, 127.5, 126.2 (d, *J* = 3.2 Hz), 125.5 (d, *J* = 7.7 Hz), 125.3,122.5, 122.2, 120.1, 115.1 (d, *J* = 21.8 Hz), 112.5 (d, *J* = 22.0 Hz), 110.2, 104.7, 69.0; HRMS (ESI+) m/z calculated for $C_{17}H_{13}FNO$ $[M+H]^+$ 266.0981, found 266.0991.

8-Nitro-6H-dibenzo[c,h]chromen-11-amine (2c)*:* Orange solid (45 mg, 78% yield), mp > 230 °C, R_f = 0.18 (40% ethyl acetate in petroleum ether, v/v); ^{1}H NMR ($CDCl_3$, 300 MHz) δ_H 8.57 (d, *J* = 8.7 Hz, 1H), 8.27-8.24 (m, 1H), 8.18 (d, *J* = 1.8 Hz, 1H), 8.11 (d, *J* = 8.4 Hz, 1H), 7.54 (d, *J* = 8.1 Hz, 1H), 7.45–7.41 (m, 1H), 7.28–7.23 (m, 1H), 6.80 (s, 1H), 5.20 (s, 2H), 4.14 (bs, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ_C 154.2, 145.9, 141.6, 136.7, 135.9, 132.6, 128.6, 125.4, 123.9, 122.9, 122.6, 120.4, 119.8, 109.4, 105.1, 68.7; HRMS (EI+) m/z calculated for $C_{17}H_{12}N_2O_3$ $[M]^+$ 292.0848, found 292.0845.

9-Chloro-6H-dibenzo[c,h]chromen-11-amine (2d)*:* Yellow solid (38.3 mg, 75% yield), mp 128–130 °C, R_f = 0.45 (40% ethyl acetate in petroleum ether, v/v); ^{1}H NMR ($CDCl_3$, 600 MHz) δ_H 8.28 (d, *J* = 8.4 Hz, 1H), 8.09 (d, *J* = 8.4 Hz, 1H), 7.54 (d, *J* = 7.8 Hz, 1H), 7.40-7.36 (m, 2H), 7.30 (d, *J* = 2.4 Hz, 1H), 7.25-7.22 (m, 1H), 6.78 (s, 1H), 5.08 (s, 2H), 4.11 (s, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ_C 152.7, 141.7, 134.9, 133.9, 132.5, 128.5, 128.4, 127.6, 125.4, 125.3, 124.9, 122.5, 122.3, 119.9, 110.0, 104.6, 68.8; HRMS (ESI+) m/z calculated for $C_{17}H_{13}ClNO$ $[M+H]^+$ 282.0686, found 282.0691.

6H-[1,3]Dioxolo[4′,5′:4,5]benzo[1,2-c]benzo[h]- chromen-12-amine (2e): Pale yellow solid (36.2 mg, 62% yield), mp 184–186 °C, R_f = 0.35 (10% ethyl acetate in petroleum ether, v/v); ^{1}H NMR ($CDCl_3$, 400 MHz) δ_H 8.05 (d, *J* = 8.4 Hz, 1H), 7.88 (s, 1H), 7.50 (d, *J* = 8.4 Hz, 1H), 7.36–7.32 (m, 1H), 7.21–7.17 (m, 1H), 6.78 (s, 1H), 6.74 (s, 1H), 5.99 (s, 2H), 4.98 (s, 2H), 4.08 (s, 2H); ^{13}C NMR($CDCl_3$, 100 MHz) δ_C 152.1, 147.8, 146.5, 141.6, 134.4, 127.2, 126.2, 125.3, 123.9, 122.4, 122.2,

120.1, 110.0, 106.2, 104.8, 104.5, 101.3, 69.4; HRMS (ESI+) m/z calculated for $C_{18}H_{14}NO_3$ $[M+H]^+$ 292.0974, found 292.1023.

9-Methyl-6H-dibenzo[c,h]chromen-11-amine (2f): Brown solid (29.3 mg, 56%), mp 168–170 °C; R_f = 0.46 (10% ethyl acetate in petroleum ether, v/v); ^{1}H NMR ($CDCl_3$, 300 MHz) δ_H 8.10 (d, J=8.1 Hz, 1H), 7.57 (d, J=8.4 Hz, 1H), 7.37 (t, J= 7.4 Hz, 1H), 7.32-7.23 (m, 3H), 7.21-7.19 (m, 1H), 6.79 (s, 1H), 5.18 (d, J=12.3 Hz, 1H), 4.81 (d, J=12.3 Hz, 1H), 3.95 (s, 2H), 2.47 (s, 3H); ^{13}C NMR($CDCl_3$, 150 MHz) δ_C 154.4, 141.7, 136.3, 134.9, 134.2, 131.9, 128.7, 127.1, 126.7, 125.2, 122.3, 122.1, 121.9, 119.4, 111.8, 102.8, 71.1, 21.7; HRMS (ESI+) m/z calculated for $C_{18}H_{16}NO$ $[M+H]^+$ 262.1232, found 262.1236.

11H-Benzo[h]thieno[2,3-c]chromen-4-amine (2h):Black gum (37.4 mg, 74% yield), R_f=0.30 (10% ethyl acetate in petroleum ether, v/v); ^{1}H NMR ($CDCl_3$, 300 MHz) δ_H 8.09 (d, J=8.4 Hz, 1H), 7.76 (d, J=5.1 Hz, 1H), 7.54 (d, J=8.1 Hz, 1H), 7.37–7.33 (m, 2H), 7.25–7.20 (m, 1H), 6.78 (s, 1H), 5.38 (s, 2H), 4.07 (brs, 2H); ^{13}C NMR($CDCl_3$, 150 MHz) δ_C 149.5, 140.9, 134.4, 131.3, 128.9, 126.9, 125.4, 124.2, 123.9, 122.5, 122.3, 120.0, 109.7, 104.4, 64.8; HRMS (ESI+) m/z calculated for $C_{15}H_{12}NOS$ $[M+H]^+$ 254.0640, found 254.0643.

2,4-Dimethoxy-12H-benzo[7,8]chromeno[3,4-d]pyrimidin-5-amine (2i): Brown solid (37.1 mg, 60% yield), mp 112–114 °C, R_f=0.20 (30% ethyl acetate in petroleum ether, v/v); ^{1}H NMR ($CDCl_3$, 300 MHz) δ_H 8.10 (d, J=8.4 Hz, 1H), 7.57 (d, J= 8.4 Hz, 1H), 7.38 (t, J=7.5 Hz, 1H), 7.26–7.21 (m, 1H), 6.85 (s, 1H), 5.02 (s, 2H), 4.17 (s, 3H), 4.07 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ_C 165.1, 164.9, 163.6, 152.2, 142.0, 134.7, 127.2, 125.1, 122.4, 122.1, 119.4, 106.9, 105.7, 104.6, 69.7, 55.1, 54.4; HRMS (ESI+) m/z calculated for $C_{17}H_{16}N_3O_3$ $[M+H]^+$ 310.1192, found 310.1205.

2,3-Dimethoxy-6H-dibenzo[c,h]chromen-11-amine (2j): Brown solid (40.5 mg, 66% yield), mp > 230 °C,R_f=0.11 (10% ethyl acetate in petroleum ether, v/v); ^{1}H NMR ($CDCl_3$, 600 MHz) δ_H 8.31 (d, J=7.8 Hz, 1H), 7.41–7.39 (m, 2H), 7.30–7.29 (m, 2H), 6.87 (s, 1H), 6.68 (s, 1H), 5.10 (s, 2H), 4.09 (s, 2H), 3.99(s, 3H), 3.98 (s, 3H); ^{13}C NMR($CDCl_3$, 150 MHz) δ_C 151.8, 150.8, 147.0, 140.8, 132.0, 130.8, 130.3, 128.4, 126.6, 125.1, 123.6, 114.5, 109.2, 104.4, 103.8, 101.4, 69.4, 55.9, 55.8; HRMS (EI+) m/z calculated for $C_{19}H_{17}NO_3$ $[M]^+$ 307.1208, found 307.1204.

2,3-Dimethoxy-8-nitro-6H-dibenzo[c,h]chromene (2k): Reddish brown solid (51.4 mg, 73% yield), mp > 250 °C, R_f =0.32 (10% ethyl acetate in petroleum ether, v/v); ^{1}H NMR ($CDCl_3$, 300 MHz) δ_H 8.55 (d, J=8.7 Hz, 1H), 8.24 (d, J=9.0 Hz, 1H),8.17 (s, 1H), 7.39 (s, 1H), 6.86 (s, 1H), 6.69 (s, 1H), 5.17 (s, 2H), 4.04 (s, 2H), 3.99 (s, 6H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ_C 152.9, 151.8, 147.4, 145.5, 140.6, 137.1, 132.2, 123.8, 123.7, 120.2, 114.2, 107.9, 104.6, 104.4, 101.5, 68.6, 55.9, 55.8; HRMS (EI+) m/z calculated for $C_{19}H_{17}N_2O_5$ $[M+H]^+$ 353.1137, found 353.1151.

3-(Trifluoromethyl)-6H-dibenzo[c,h]chromen-11-amine (2l): Brown gum (25.2 mg, 42% yield), R_f=0.27 (10% ethyl acetate in petroleum ether, v/v); ^{1}H NMR ($CDCl_3$, 300 MHz) δ_H 8.40 (s, 1H), 8.27 (d, J=7.8 Hz, 1H), 7.58 (d, J=8.4 Hz, 1H), 7.50 (d, J=8.7 Hz, 1H), 7.43–7.40 (m, 1H), 7.35–7.33 (m, 1H), 6.78 (s, 1H), 5.15 (s, 2H), 4.37(s, 2H); ^{13}C NMR($CDCl_3$, 150 MHz) δ_C 153.4, 144.0, 135.9, 132.1, 129.3, 129.0, 128.5, 127.4, 125.8, 125.4, 123.7, 123.3, 122.8 (m), 120.4 (m), 118.6, 111.3, 103.7, 69.4; HRMS (ESI+) m/z calculated for $C_{18}H_{12}F_3O$ $[M+H]^+$ 301.0840, found 301.0838.

2-Fluoro-6H-dibenzo[c,h]chromen-11-amine (2m) : Pale yellow solid (33.5 mg, 63% yield), mp 130–132 °C, R_f=0.36 (10% ethyl acetate in petroleum ether, v/v); ^{1}H NMR ($CDCl_3$, 300 MHz) δ_H 8.27 (d, J=7.8 Hz, 1H), 8.11-8.06 (m, 1H), 7.43–7.38 (m, 1H), 7.31(d, J=4.2 Hz, 2H), 7.13 (dd, J=10.5, 2.1 Hz, 1H), 6.96 (td, J=8.7, 2.4 Hz, 1H), 6.69 (s, 1H), 5.11 (s, 2H), 4.25 (s, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ_C 162.2 (d, J= 244.6 Hz), 153.0, 143.2, 136.0 (d, J=9.9 Hz), 132.0, 129.7, 128.5, 127.0, 125.3, 125.0 (d, J=9.6 Hz), 123.4, 116.9, 112.2 (d, J=25.0 Hz), 109.8, 108.3 (d, J=21.3 Hz), 103.4 (d, J= 5.1 Hz), 69.4; HRMS (ESI+) m/z calculated for $C_{17}H_{13}FNO$ $[M+H]^+$ 266.0981, found 266.0988.

Spectral data of Products 12–13

2,3,4,6-Tetrahydro-1H-benzo[c]chromen-1-one (12): White solid (26 mg, 65% yield); mp 122–124 °C; R_f=0.29 (10% ethyl acetate in petroleum ether, v/v); ^{1}H NMR ($CDCl_3$, 600 MHz) δ_H 8.29 (d, J=7.8 Hz, 1H), 7.32 (t, J=7.5 Hz, 1H), 7.21 (t, J= 7.5 Hz, 1H), 7.03 (d, J=7.2 Hz, 1H), 5.12 (s, 2H), 2.58–2.54 (m, 4H), 2.03–1.99 (m, 2H); ^{13}C NMR($CDCl_3$, 150 MHz) δ_C 196.5, 174.1, 128.6, 127.8, 127.0, 126.9, 124.8, 123.7, 113.1, 69.5, 38.3, 28.9, 20.1; HRMS (EI+) m/z calculated for $C_{13}H_{12}O_2$ $[M]^+$ 200.0837, found 200.0839.

9-Chloro-2,3,4,6-tetrahydro-1H-benzo[c]chromen-1-one (13): Pale yellow solid (32.8 mg, 70% yield), mp 164–166 °C, R_f = 0.28 (10% ethyl acetate in petroleum ether, v/v); ^{1}H NMR ($CDCl_3$, 300 MHz) δ_H 8.36 (t, J=1.8 Hz, 1H), 7.19–7.16 (m, 1H), 6.95 (d, J=8.1 Hz, 1H), 5.09 (s, 2H), 2.59–2.51 (m, 4H), 2.04–1.96 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ_C 196.2, 174.9, 134.4, 129.3, 126.7, 125.0, 124.9, 124.8, 112.1, 68.9, 38.1, 28.9, 19.9; HRMS (ESI+) m/z calculated for $C_{13}H_{12}ClO_2$ $[M+H]^+$ 235.0526, found 235.0522.

General Procedure for the Synthesis of 6*H*-dibenzo [*c,h*]chromenes 2′

A mixture of $Pd(OAc)_2$bpy (3.8 mg, 0.01 mmol, 5 mol%) and D-CSA (69.6 mg, 0.3 mmol, 1.5 equiv.) in dry 1,4-dioxane (2 mL) was stirred at 90 °C for 5 min under argon atmosphere. Next the starting material **10′** (0.20 mmol) dissolved in 1,4-dioxane (1.5 mL) was added to the reaction mixture at the same temperature and the whole mixture was allowed to stir at heating conditions (100 °C) for few hours until the completion of the reaction (TLC). Thereafter, the reaction mixture was neutralized by adjusting the pH (~7) through drop wise addition of 20% aqueous sodium bicarbonate solution and extracted with ethyl acetate (3×20 mL). The combined organic extracts were washed with saturated brine (10 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The resulting residue was purified through silica gel (100-200 mesh) column chromatography using 0–20% ethyl acetate-petroleum ether (v/v) as eluent to afford desired product **2′**in 47–86% yield.

6H-Dibenzo[c,h]chromene (2′a): Yellow solid (39.9 mg, 86% yield), mp 100–102 °C, R_f = 0.46 (petroleum ether); ^{1}H NMR ($CDCl_3$, 600 MHz) δ_H 8.28-8.26 (m, 1H), 7.85 (d, J = 8.4 Hz, 1H), 7.82–7.80 (m, 1H), 7.75 (d, J = 7.8 Hz, 1H), 7.55 (d, J = 8.4 Hz, 1H), 7.50–7.48 (m, 2H), 7.42 (t, J = 7.8 Hz 1H), 7.31 (t, J = 7.5 Hz, 1H), 7.23 (d, J = 7.2 Hz, 1H), 5.32 (s, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ_C 150.3, 134.4, 130.8, 130.7, 128.6, 127.6, 127.4, 126.6, 125.8, 125.3, 124.6, 122.3, 121.9, 121.6, 120.9, 117.2, 68.9; HRMS (ESI+) m/z calculated for $C_{17}H_{13}O$ $[M+H]^+$ 233.0966, found 233.0944.

8-Nitro-6H-dibenzo[c,h]chromene (2′b): Yellow solid (30.0 mg, 56% yield); mp 158–160 °C; R_f = 0.63 (10% ethyl acetate in petroleum ether, v/v); ^{1}H NMR ($CDCl_3$, 600 MHz) δ_H 8.29-8.27 (m, 2H), 8.12 (d, J = 2.4 Hz, 1H), 7.85 (d, J = 8.4 Hz,1H), 7.84–7.82 (m, 2H), 7.58(d, J = 8.4 Hz, 1H), 7.57-7.53 (m, 2H), 5.40 (s, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ_C 151.9, 146.6, 137.3, 135.4 131.3, 127.9, 127.8, 126.4, 125.1, 124.1, 122.6, 122.5, 122.4, 120.8, 120.2, 115.3, 68.3; HRMS (ESI+) m/z calculated for $C_{17}H_{12}NO_3$ $[M+H]^+$ 278.0817, found 278.0814.

8-Fluoro-6H-dibenzo[c,h]chromene (2′c): White solid (39.5 mg, 79% yield), mp 158–160 °C, R_f = 0.54 (petroleum ether); ^{1}H NMR ($CDCl_3$, 600 MHz) δ_H 8.27–8.26 (m, 1H), 7.82-7.81 (m, 1H), 7.78(d, J = 8.4 Hz, 1H), 7.70-7.68 (m, 1H), 7.55 (d, J = 8.4 Hz, 1H), 7.52-7.49(m, 2H), 7.11(td, J = 8.55, 2.8 Hz, 1H), 6.94 (dd, J = 8.4, 2.4 Hz, 1H), 5.28 (s, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ_C 162.3 (d, J = 246 Hz), 149.8, 134.2, 132.9 (d, J = 7.5 Hz), 127.7, 126.9, 126.7, 125.9, 125.3, 123.8 (d, J = 9 Hz), 122.2, 121.8, 120.7, 116.6, 115.4 (d, J = 22.5 Hz), 111.9 (d, J = 22.5 Hz), 68.4; HRMS (ESI+) m/z calculated for $C_{17}H_{12}FO$ $[M+H]^+$ 251.0872, found 251.0876.

9-Chloro-6H-dibenzo[c,h]chromene (2′d): Yellow solid (43.1 mg, 81% yield), mp 101–103 °C, R_f = 0.49 (petroleum ether); ^{1}H NMR ($CDCl_3$, 400 MHz) δ_H 8.27-8.25 (m, 1H), 7.82-7.78 (m, 1H), 7.73 (d, J = 8.8 Hz, 1H), 7.68 (d, J = 2 Hz, 1H), 7.52–7.48 (m, 3H), 7.24 (dd, J = 2 Hz,1H), 7.10 (d, J = 8 Hz, 1H), 5.24 (s, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ_C 150.7, 134.8, 134.6, 132.6, 128.9, 127.8, 127.2, 127.1, 126.1, 125.9, 125.3, 122.4, 122.2, 121.9, 120.8, 116.1, 68.4; HRMS (ESI+) m/z calculated for $C_{17}H_{12}ClO$ $[M+H]^+$ 267.0577, found 267.0573.

8-Bromo-6H-dibenzo[c,h]chromene (2′e): White solid (47.1 mg, 76% yield), mp 140–142 °C, R_f = 0.54 (petroleum ether); ^{1}H NMR ($CDCl_3$, 600 MHz) δ_H 8.26-8.24 (m, 1H), 7.81–7.79 (m, 1H), 7.78 (d, J = 8.4 Hz, 1H), 7.60 (d, J = 8.4 Hz, 1H), 7.55–7.52 (m, 2H), 7.51–7.49 (m, 2H), 7.37 (s, 1H), 5.27 (s, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ_C 150.3, 134.5, 132.6, 131.6, 129.8, 127.7, 126.9, 126.0, 125.3, 123.6, 122.3, 121.8, 121.0, 120.6, 116.3, 68.2; HRMS (ESI+) m/z calculated for $C_{17}H_{12}BrO$ $[M+H]^+$ 311.0072, found 311.0066.

2,3-Dimethoxy-6H-dibenzo[c,h]chromene (2′g): Yellow solid (43.8 mg, 75% yield), mp 140–144 °C, R_f = 0.55 (20% ethyl acetate in petroleum ether, v/v); ^{1}H NMR ($CDCl_3$, 600 MHz) δ_H 7.73–7.71 (m, 2H), 7.54 (s, 1H), 7.42–7.39 (m, 2H), 7.28 (td, J = 1.0, 7.35 Hz, 1H), 7.21 (d, J = 7.2 Hz, 1H), 7.11 (s, 1H), 5.29 (s, 2H), 4.05 (s, 3H), 4.02 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ_C 150.1, 149.44, 149.42, 130.9, 130.5, 130.4, 128.5, 127.0, 124.6, 121.8, 120.4, 120.1, 119.4, 116.1, 106.4, 101.1, 68.9, 55.99, 55.91; HRMS (ESI+) m/z calculated for $C_{19}H_{17}O_3$ $[M+H]^+$ 293.1178, found 293.1174.

2-Fluoro-6H-dibenzo[c,h]chromene (2′h): Yellow solid (31 mg, 62% yield), mp 118–120 °C, R_f = 0.54 (petroleum ether); ^{1}H NMR ($CDCl_3$, 600 MHz) δ_H 8.29-8.26 (m, 1H), 7.86 (d, J = 8.4 Hz, 1H), 7.73 (d, J = 7.8 Hz, 1H), 7.46 (d, J = 8.4 Hz, 1H), 7.43–7.41 (m, 2H), 7.31 (t, J = 7.5 Hz 1H), 7.28–7.24 (m, 1H), 7.22 (d, J = 7.2 Hz, 1H), 5.31 (s, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ_C 161.4(d, J = 246 Hz), 150.5, 135.4 (d, J = 9 Hz), 130.4 (d, J = 4.5 Hz), 128.6, 127.5, 125.1(d, J = 10.5 Hz), 124.7,122.4, 121.8, 120.8(d, J = 4.5 Hz), 116.6 (d, J = 1.5 Hz), 115.9, 115.8, 111.0, 110.9, 68.9; HRMS (ESI+) m/z calculated for $C_{17}H_{12}FO$ $[M+H]^+$ 251.0872, found 251.0871.

4-Methyl-6H-dibenzo[c,h]chromene (2′i): Yellow solid (23.1 mg, 47% yield), mp 70–72 °C, R_f = 0.56 (petroleum ether); ^{1}H NMR ($CDCl_3$, 600 MHz) δ_H 7.82 (d, J = 8.4 Hz, 1H), 7.74 (d, J = 7.8 Hz, 1H), 7.63 (d, J = 8.4 Hz, 1H), 7.53 (d, J = 8.4 Hz, 1H), 7.43 (t, J = 7.5 Hz, 1H), 7.33-7.30 (m, 2H), 7.24–7.22 (m, 2H), 5.23 (s, 2H), 2.94 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ_C 152.8, 135.9, 135.6, 131.0, 130.8, 128.8, 128.6, 127.2, 126.4, 126.2, 125.1, 124.4, 122.6, 122.3, 121.1, 118.5, 68.2, 25.2; HRMS (ESI+) m/z calculated for $C_{18}H_{15}O$ $[M+H]^+$ 247.1123, found 247.1122.

12-Methyl-6H-dibenzo[c,h]chromene (2′j): Yellow gum (40.8 mg, 83% yield),R_f = 0.44 (petroleum ether);^{1}H NMR ($CDCl_3$, 600 MHz) δ_H 8.31 (d, J = 9 Hz, 1H), 7.95 (d, J = 8.4 Hz, 1H), 7.76 (d, J = 7.2 Hz, 1H), 7.69 (s, 1H), 7.56–7.51 (m, 2H), 7.42 (t, J = 7.5 Hz, 1H), 7.30 (t, J = 7.5 Hz, 1H), 7.22 (d, J = 7.8 Hz, 1H), 5.30 (s, 2H), 2.71 (s, 3H); ^{13}C NMR($CDCl_3$, 150 MHz) δ_C 148.9, 133.4, 130.9, 130.7, 128.5, 127.6, 127.3, 126.5, 125.54, 125.5, 124.6, 124.2, 122.7, 121.9, 121.3, 116.6, 68.9, 19.3; HRMS (ESI+) m/z calculated for $C_{18}H_{15}O$ $[M+H]$ + 247.1123, found 247.1125.

Synthesis of 6*H*-dibenzo[*c,h*]chromen-6-ones (3) from 6*H*-dibenzo[*c,h*]chromenes 2′ by benzylic oxidation

To a solution of 2′(0.086 mmol, 1 equiv.) in dry DCM was added PCC (27.7 mg, 0.13 mmol, 1.5 equiv.) and heated at refluxing temperature for 3–4 h until complete consumption of the starting material (TLC).The crude product was filtered through a plug of silicagel (100-200 mesh size) which was washed with DCM, and the solution was concentrated *in vacuo*. The crude product was purified through silica gel (100-200 mesh) column chromatography eluting with 18–20% ethyl acetate-petroleum ether (v/v) to furnish the pure product 3 in 64–95% yield.

6H-Dibenzo[c,h]chromen-6-one (3a): White solid (19.4 mg, 92% yield), mp 188–190 °C, R_f = 0.53 (10% ethyl acetate in petroleum ether, v/v); ^{1}H NMR ($CDCl_3$, 300 MHz) δ_H 8.59 (d, J = 7.5 Hz, 1H), 8.47 (d, J = 7.8 Hz, 1H), 8.19 (d, J = 8.1 Hz, 1H), 8.06(d, J = 9.0 Hz, 1H), 7.89–7.85 (m, 2H), 7.77 (d, J = 8.7 Hz, 1H), 7.66-7.58 (m, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ_C 161.3, 147.3, 135.5, 135.0, 134.3, 130.7, 128.7, 127.9, 127.7, 127.2, 124.6, 123.9, 122.4, 122.1, 121.2, 119.2, 113.1; HRMS (ESI+) m/z calculated for $C_{17}H_{11}O_2$ $[M+H]^+$ 247.0759, found 247.0764.

8-Fluoro-6H-dibenzo[c,h]chromen-6-one (3b): White solid (17.9 mg, 79% yield), mp 219–221 °C,R_f = 0.55 (10% ethyl acetate in petroleum ether, v/v); ^{1}H NMR ($CDCl_3$, 600 MHz) δ_H 8.55 (d, J = 8.4 Hz, 1H), 8.19.–8.17 (m, 1H), 8.10 (dd, J = 3, 8.4 Hz, 1H), 7.99 (d, J = 8.4 Hz, 1H), 7.87 (d, J = 7.8 Hz, 1H), 7.77 (d, J = 9.0 Hz, 1H), 7.65–7.56 (m, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ_C 162.3 (d, J = 249 Hz), 160.3 (d, J = 3 Hz), 146.7, 134.1, 131.9 (d, , J = 3 Hz), 127.8 (d, J = 39 Hz), 127.3, 124.8, 124.6 (d, J = 9 Hz), 123.8, 123.3, 123.2, 122.9 (d, J = 9 Hz), 122.2, 118.9, 116.2(d, J = 22.5 Hz), 112.4; HRMS (ESI+) m/z calculated for $C_{17}H_{10}FO_2$ $[M+H]^+$ 265.0665, found 265.0644.

12-Methyl-6H-dibenzo[c,h]chromen-6-one (3c): White solid (21.2 mg, 95% yield), mp 195–197 °C, R_f = 0.58 (10% ethyl acetate in petroleum ether, v/v); ^{1}H NMR ($CDCl_3$, 600 MHz) δ_H 8.63-8.61 (m, 1H), 8.47 (d, J = 7.8 Hz, 1H), 8.19 (d, J = 7.8 Hz, 1H), 8.01-7.99 (m, 1H), 7.88–7.85(m, 2H), 7.66–7.65 (m, 2H), 7.60 (t, J = 7.5 Hz, 1H), 2.76 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ_C 161.4, 146.0, 135.4, 134.9, 133.4, 130.8, 130.6, 128.5, 127.7, 126.8, 124.2, 123.9, 122.8, 121.9, 121.3, 119.2, 112.5, 19.5; HRMS (ESI+) m/z calculated for $C_{18}H_{12}NaO_2$ $[M+Na]^+$ 283.0735, found 283.0740.

2,3-Dimethoxy-6H-dibenzo[c,h]chromen-6-one (3d): White solid (16.8 mg, 64% yield), mp 176–178 °C, R_f = 0.57 (10% ethyl acetate in petroleum ether, v/v); ^{1}H NMR ($CDCl_3$, 300 MHz) δ_H 8.44 (d, J = 7.8 Hz, 1H), 8.14 (d, J = 8.1 Hz, 1H), 7.91 (d, J = 8.7 Hz, 1H), 7.84 (t, J = 7.2 Hz, 1H), 7.79 (s, 1H), 7.61–7.54 (m, 2H), 7.14 (s, 1H), 4.10 (s, 3H), 4.03 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ_C 161.6, 150.9, 150.3, 146.5, 135.8, 134.9, 130.6, 130.4, 128.2, 122.9, 121.8, 120.7, 119.0, 117.6, 111.9, 106.4, 101.1, 56.4, 56.0; HRMS (ESI+) m/z calculated for $C_{19}H_{15}O_4$ $[M+H]^+$ 307.0970, found 307.0974.

General procedure for the synthesis of 2,4-dimethoxy-12*H*-benzo[7,8]chromeno[3,4-*d*]pyrimi- dine 16

A mixture of $Pd(OAc)_2$bpy (5.7 mg, 0.015 mmol, 5 mol%), D-CSA (139.2 mg, 0.6 mmol, 2 equiv.) in dry NMA (2 mL) was stirred at 90 °C for 5 min under argon atmosphere. The substrate **14** (0.3 mmol, 1 equiv.) dissolved in NMA (1.0 mL) was then added dropwise and the whole mixture was allowed to stir at 100 °C for few hours until completion of the reaction (TLC). Thereafter, the reaction mixture was neutralized by adjusting the pH (~7) through drop wise addition of 20% aqueous sodium bicarbonate solution and then extracted with ethyl acetate (3 × 20 mL). The combined organic extracts were washed with saturated brine (10 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The resulting residue was purified through silica gel (100-200 mesh) column chromatography using 15–20% ethyl acetate-petroleum ether (v/v) as eluent to afford desired product **16** in 50–65% yield.

2,4-Dimethoxy-12H-benzo[7,8]chromeno[3,4-d]pyrimidine (16a): Pale yellow solid (49.4 mg, 56% yield), mp 119–121 °C, R_f = 0.43 (20% ethyl acetate in petroleum ether, v/v); ^{1}H NMR ($CDCl_3$, 600 MHz) δ_H7.84 (d, J = 1.2 Hz, 1H), 7.57 −7.55 (m,2H), 7.45 (d, J = 7.8 Hz, 1H), 7.27–7.24 (m, 1H), 7.19 (t, J = 7.5 Hz, 1H), 5.14 (s, 2H), 4.14 (s, 3H), 4.05(s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ_C 168.7, 162.8, 160.9, 150.6, 140.7, 136.7, 129.7, 126.6, 126.3, 124.7, 121.3, 117.5, 111.4, 87.9, 85.9, 55.0, 54.6; HRMS (ESI+) m/z calculated for $C_{17}H_{15}N_2O_3$ $[M+H]^+$ 295.1083, found 295.1086.

8-Fluoro-2,4-dimethoxy-12H-benzo[7,8]chromeno [3,4-d]pyrimidine (16b): Pale yellow solid (61.0 mg, 65% yield), mp 158–160 °C, R_f = 0.41 (20% ethyl acetate in petroleum ether, v/v); ^{1}H NMR ($CDCl_3$, 600 MHz) δ_H 7.80 (d, J = 1.2 Hz, 1H), 7.52 (s, 1H), 7.37–7.35 (m, 1H), 7.23 (dd, J = 2.1,9.3 Hz, 1H), 6.98–7.95 (m, 1H), 5.15 (s, 2H), 4.15 (s, 3H), 4.05 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ_C 168.7, 161.8 (d, J = 209.4 Hz), 151.3, 138.5(d, J = 9 Hz), 136.8 (d, J = 2.2 Hz), 128.9 (d, J = 1.5 Hz), 122.1, 122.0, 121.6, 113.5 (d,J = 23.3 Hz), 111.4, 105.1, 104.9, 77.3, 55.1, 54.7; HRMS (ESI+) m/z calculated for$C_{17}H_{14}FN_2O_3$ $[M+H]+$ 313.0988, found 313.0991.

2,4,8,9-Tetramethoxy-12H-benzo[7,8]chromeno[3,4-d]pyrimidine (16c): Pale yellow solid (53.1 mg, 50% yield), mp 212–214 °C, R_f = 0.19 (20% ethyl acetate in petroleum ether, v/v); ^{1}H NMR ($CDCl_3$, 600 MHz) δ_H 8.08 (d, J = 9.0 Hz, 1H), 7.50 (s, 1H), 7.37 (d, J = 8.4 Hz, 1H), 7.09 (s, 1H), 5.19 (s, 2H), 4.15 (s, 3H), 4.04 (s, 3H) 4.03 (s, 3H), 4.01(s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ_C 166.6, 163.5, 161.4, 150.1, 149.4, 148.1, 129.8, 122.5, 119.9, 119.8, 111.9, 106.1, 105.8, 100.8, 69.2, 56.0, 55.9, 54.9, 54.3; HRMS (ESI+) m/z calculated for $C_{19}H_{19}N_2O_5$ $[M+H]^+$ 355.1294, found 355.1299.

General procedure for the synthesis of 8,9-dimethoxy-1*H*-benzo[7,8]chromeno[3,4-*d*]pyri- mi- dine-2,4(3*H*,12*H*)-dione (17)

To a well stirred and ice-cooled solution of **16c** (30 mg, 0.08, 1 equiv.) in dry acetonitrile (3 mL) were added anhydrous sodium iodide (35.7 mg, 0.24 mmol, 3 equiv.) and freshly distilled trimethylsilylchloride (30 µL, 0.24 mmol, 3 equiv.) successively. The reaction mixture was then stirred at room temperature until the complete conversion of the starting material (TLC). The solvent was removed under reduced pressure; the crude product was filtered, and washed with ethyl acetate several times. The resulting yellow solid was dried *in vacuo* to afford the product **17**.

8,9-Dimethoxy-1H-benzo[7,8]chromeno[3,4-d]pyri- midine-2,4 (3H,12H)-dione (17): Pale yellow solid (16.4 mg, 58% yield), mp >260 °C; ^{1}H NMR (DMSO-d_6, 600 MHz) δ_H 11.40 (s, 1H), 11.31 (s, 1H), 8.30 (d, J = 9 Hz, 1H), 7.37 (d, J = 9 Hz, 1H), 7.29 (s, 1H), 7.24 (s,1H),5.03 (s, 2H), 3.85 (s, 6H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ_C 162.1, 150.7, 149.9, 149.7, 145.4, 144.9,129.2, 121.2, 119.9, 119.2, 113.2, 106.9, 101.2, 100.3, 63.9, 55.9, 55.8; HRMS (ESI+) m/z calculated for $C_{17}H_{15}N_2O_5$ $[M+H]^+$ 327.0981, found 327.0990.

Synthesis of 2,3-dimethoxy-5-tosyl-5,6-dihydrobenzo[*c*]phenanthridin-11-amine 4a

A mixture of $Pd(OAc)_2$ (2.5 mg, 0.011 mmol, 5 mol%), phenanthroline (2.38 mg, 0.013 mmol, 6 mol%) and D-CSA (76 mg, 0.33 mmol, 1.5 equiv.) in NMA(3 mL) was stirred at reflux temperature for 5 min under argon atmosphere. Then the starting material **18** (0.22 mmol) dissolved in NMA (1.5 mL) was added to the reaction mixture at the same temperature and the whole mixture was allowed to stir at 95 °C for few hours until the completion of the reaction (TLC). The reaction mixture

was then neutralized by adjusting the pH (~7) through drop wise addition of 20% aqueous sodium bicarbonate solution and extracted with ethyl acetate (3×20 mL). The combined organic extracts were washed with saturated brine (10 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The resulting residue was purified through silica gel (100–200 mesh) column chromatography using eluent 30% ethyl acetate-petroleum ether (v/v) to afford the desired product **4a**.

2,3-Dimethoxy-5-tosyl-5,6-dihydrobenzo[c]phenan- thridin-11-amine (4a): Brown solid (74.9 mg, 74% yield), mp 186–188 °C, R_f = 0.46 (50% ethyl acetate in petroleum ether, v/v); ^{1}H NMR ($CDCl_3$, 600 MHz) δ_H 7.98 (s, 1H), 7.41 (d, J= 7.8 Hz, 1H), 7.23 (d, J=7.8 Hz, 1H), 7.12 (t, J=7.8 Hz, 1H), 7.02-6.99 (m, 2H), 6.88 (s, 1H), 6.73 (d, J=8.4 Hz, 2H), 7.68 (d, J=7.8 Hz, 2H), 5.21 (d, J=15.2 Hz, 1 Hz), 4.37 (d,J= 16.2 Hz, 1H), 4.09 (s, 3H), 4.00 (s, 3H), 2.19 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ_C 150.9, 147.5, 142.3, 139.7, 133.8, 133.7, 133.5, 131.4, 130.8, 128.3, 127.2, 127.1, 126.8, 126.6, 125.3, 120.9, 119.0, 110.9, 106.1, 103.7, 56.1, 55.8, 52.1, 21.3; HRMS (ESI+) m/z calculated for $C_{26}H_{25}N_2O_4S$ $[M+H]^+$ 461.1535, found 461.1550.

General procedure of synthesis of 5-tosyl-5,6-dihydrobenzo[*c*]phenanthridine

A mixture of $Pd(OAc)_2$bpy (3.8 mg, 0.01 mmol, 5 mol%), and D-CSA (69.6 mg, 0.3 mmol, 1.5 equiv.) in dry THF (1 mL) was stirred at 60 °C under argon atmosphere. Then the starting material **10′** (0.2 mmol) dissolved in dry THF (1 mL) was added to the reaction mixture at the same temperature and the whole mixture was allowed to stir at reflux temperature for few hours until the completion of the reaction (TLC). Thereafter the reaction mixture was neutralized by adjusting the pH (~7) through drop wise addition of 20% aqueous sodium bicarbonate solution and extracted with ethyl acetate (3×20 mL). The combined organic extracts were washed with saturated brine (10 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The resulting residue was purified through silica gel (100-200 mesh) column chromatography using eluent 10–40% ethyl acetate-petroleum ether (v/v) to afford desired product **4′**.

5-Tosyl-5,6-dihydrobenzo[c]phenanthridine (4′a): Yellow solid (60.1 mg, 78% yield), mp 154–156 °C, R_f = 0.44 (5% ethyl acetate in petroleum ether, v/v); ^{1}H NMR ($CDCl_3$, 400 MHz) δ_H 8.72 (d, J=8.4 Hz, 1H), 7.85-7.82 (m, 2H), 7.64-7.60 (m, 2H), 7.55-7.51 (m, 1H), 7.20 (d, J=7.6 Hz, 1H), 7.14-7.04 (m, 3H), 6.80 (d, J=8.0 Hz, 2H), 6.64 (d, J=8.4 Hz, 2H), 5.29 (d, J= 16.4 Hz, 1H), 4.53 (d, J=16.4 Hz, 1H), 2.16 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ_C 142.9, 133.9, 133.7, 132.5, 132.2, 132.0, 131.5, 129.3, 128.6, 128.2, 127.9, 127.6, 127.5, 127.4, 126.9, 126.8, 126.5, 126.2, 123.2, 121.4, 51.2, 21.4; HRMS (ESI+) m/z calculated for $C_{24}H_{20}NO_2S$ $[M+H]^+$ 386.1215, found 386.1201.

Methyl 5-tosyl-5,6-dihydrobenzo[c]phenanthridine-8-carboxy-late(4′b): Brown solid (47.8 mg, 54% yield), mp 106–108 °C, R_f = 0.22 (5% ethyl acetate in petroleum ether, v/v); ^{1}H NMR ($CDCl_3$, 600 MHz) δ_H 8.74 (d, J=9.0 Hz, 1H), 7.90-7.86 (m, 2H), 7.77–7.75 (m, 2H), 7.68–7.65 (m, 2H), 7.60–7.58 (m, 1H), 7.32 (d, J=8.4 Hz, 1H), 6.85 (d, J=8.4 Hz, 2H), 6.67 (d, J= 7.8 Hz, 2H), 5.35 (d, J=16.8 Hz, 1H), 4.58 (d, J=16.8 Hz, 1H), 3.97 (s, 3H), 2.17 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ_C 166.5, 143.3, 136.2, 134.4, 133.6, 133.57, 132.2, 131.4, 129.2, 128.8, 128.7, 128.4, 128.1, 127.7, 127.5, 127.4, 127.3, 127.0, 126.8, 123.1, 121.3, 52.4, 50.8, 21.3; HRMS (ESI+) m/z calculated for $C_{26}H_{22}NO_4S$ $[M+H]^+$ 444.1270, found 444.1270.

9-Chloro-5-tosyl-5,6-dihydrobenzo[c]phenanthri- dine (4′c): Yellow solid (67.9 mg, 81% yield), mp 140–142 °C, R_f=0.46 (5% ethyl acetate in petroleum ether, v/v); ^{1}H NMR ($CDCl_3$, 600 MHz) δ_H 8.74 (d, J=8.4 Hz, 1H), 7.89–7.86 (m, 2H), 7.67-7.64 (m, 1H), 7.59–7.55 (m, 2H), 7.15–7.13 (m, 2H), 7.07 (d, J=8.4 Hz, 1H), 6.78 (d, J=8.4 Hz, 2H), 6.75 (d, J=7.8 Hz, 2H), 5.29 (d, J=16.2 Hz, 1H), 4.48 (d, J=16.2 Hz, 1H), 2.28 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ_C 143.6, 134.2, 133.8, 133.7, 132.9, 131.3, 130.4, 128.8, 128.3, 128.2, 127.6, 127.5, 127.4, 127.2, 126.9, 126.8, 123.4, 121.1, 50.6, 21.4; HRMS (ESI+) m/z calculated for $C_{24}H_{19}ClNO_2S$ $[M+H]+$ 420.0825, found 420.0823.

12-Tosyl-12,13-dihydro-[1,3]dioxolo[4′,5′:4,5]ben-zo[1,2-c] phenanthridine (4′d): Pale yellow solid (36.1 mg, 42% yield), mp 74–78 °C, R_f = 0.55 (20% ethyl acetate in petroleum ether, v/v); ^{1}H NMR ($CDCl_3$, 600 MHz) δ_H 8.05 (s, 1H), 7.66 (d, J= 8.4 Hz, 1H), 7.46 (d, J=8.4 Hz,1H), 7.15 (d, J=7.8 Hz, 1H), 7.11-7.10 (m, 3H), 7.05-7.03 (m, 1H), 6.81(d, J=7.8 Hz, 2H), 6.66 (d, J=7.8 Hz, 2H), 6.09 (d, J=8.4 Hz, 2H), 5.27 (d, J= 16.8 Hz, 1H), 4.50 (d, J=16.2 Hz, 1H), 2.17 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ_C 148.4, 142.8, 133.4, 132.2, 131.9, 131.7, 131.4, 128.9, 128.2, 128.0, 127.6, 127.57, 127.4, 127.37, 126.1, 122.9, 119.9, 103.5, 103.3, 101.4, 51.2, 21.3; HRMS (ESI+) m/z calculated for $C_{25}H_{20}NO_4S$ $[M+H]^+$ 430.1113, found 430.1125.

2-Fluoro-5-tosyl-5,6-dihydrobenzo[c]phenanthri- dine (4′e): Yellow solid (54.0 mg, 67% yield), mp 140–142 °C, R_f= 0.37 (5% ethyl acetate in petroleum ether, v/v); ^{1}H NMR ($CDCl_3$, 600 MHz) δ_H 8.75–8.73 (m, 1H), 7.79 (d, J=8.4 Hz, 1H), 7.66 (d, J=8.4 Hz, 1H), 7.45 (dd, J=9.0, 2.4 Hz, 1H), 7.42–7.38 (m, 1H), 7.20 (d, J=7.8 Hz, 1H), 7.16-7.07 (m, 3H), 6.81 (d, J=8.4 Hz, 2H), 6.67 (d, J=7.8 Hz, 2H), 5.30 (d, J=16.8 Hz, 1H), 4.55 (d, J=16.2 Hz, 1H), 2.18 (s, 3H);^{13}C NMR ($CDCl_3$, 100 MHz) δ_C 161.4 (d, J=247 Hz), 143.1, 134.9 (d, J=10 Hz), 133.5, 132.7 (d, J=2 Hz), 131.9, 131.7, 129.9, 129.8, 128.6 (d, J=2 Hz), 128.5 (d, J=2 Hz), 128.3, 128.1, 127.7 (d, J=5 Hz), 127.60?, 127.57, 126.3, 123.1, 122.7, 116.8 (d, J=25 Hz), 110.5 (d, J=21 Hz), 51.1, 21.4; HRMS (ESI+) m/z calculated for $C_{24}H_{18}FNNaO_2S$ $[M+Na]+$ 426.0940, found 426.0942.

9-Bromo-5-tosyl-5,6-dihydrobenzo[c]phenanthri- dine (4′f): Yellow solid (51.9 mg, 56% yield), mp 140–142 °C, R_f=0.41 (5% ethyl acetate in petroleum ether, v/v); ^{1}H NMR ($CDCl_3$, 300 MHz) δ_H 8.60 (d, J=9.0 Hz, 1H), 8.00 (d, J=1.5 Hz, 1H), 7.76 (d, J=8.4 Hz, 1H), 7.71–7.64 (m, 2H), 7.20 (d, J=7.5 Hz, 1H), 7.16–7.06 (m, 3H), 6.80 (d, J=8.4 Hz, 2H), 6.66 (d, J= 8.1 Hz, 2H), 5.30 (d, J=16.8 Hz, 1H), 4.54 (d, J=16.8 Hz, 1H), 2.17 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ_C 143.0, 134.9, 133.3, 132.6, 132.1, 131.5, 130.0, 129.9, 129.5, 129.4, 128.8, 128.3, 128.2, 127.56, 127.55, 127.5, 126.3, 123.1, 122.6, 121.2, 51.0, 21.3; HRMS (ESI+) m/z calculated for $C_{24}H_{19}BrNO_2S$ $[M+H]^+$ 464.0320, found 464.0236.

Synthesis of Benzo[*c*]phenanthridine 19

To a solution of compound **4′** (0.13 mmol,1 equiv.)in dry DMSO (3 mL)was added finely ground KOH pellets (36.4 mg, 0.65 mmol, 5 equiv.) and the reaction was allowed to stir at room temperature for 1–2 h. After completion of the reaction (TLC), the reaction mixture was diluted with water (8 mL) and extracted with ethyl acetate (3 × 15 mL). The combined organic layers were dried over anhydrous sodium sulphate, filtered and concentrated under reduced pressure. The resulting crude product was purified by silica gel (100–200 mesh) column chromatography with 4–5%ethyl acetate-pet ether (v/v) as eluent to afford the pure products **19** in 51–79% yield.

Benzo[c]phenanthridine (19a): White solid (15.2 mg, 51% yield), mp 99–101 °C, R_f = 0.40 (5% ethyl acetate in petroleum ether, v/v); ^{1}H NMR ($CDCl_3$, 600 MHz) δ_H 9.51 (s, 1H), 9.42 (d, J = 8.4 Hz, 1H), 8.72 (d, J = 8.4 Hz, 1H), 8.59 (d, J = 8.4 Hz, 1H), 8.18 (d, J = 7.8 Hz, 1H), 8.07 (d, J = 8.4 Hz, 1H), 8.01 (d, J = 7.8 Hz, 1H), 7.92 (t, J = 7.8 Hz, 1H), 7.80–7.75 (m, 2H), 7.71 (t, J = 7.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ_C 152.1, 141.5, 133.3, 132.9, 132.1, 130.9, 128.8, 127.9, 127.7, 127.4, 127.2, 127.1, 126.9, 124.7, 122.3, 121.1, 119.9; HRMS (ESI+) m/z calculated for $C_{17}H_{12}N$ $[M+H]^+$ 230.0970, found 230.0969.

9-Chlorobenzo[c]phenanthridine (19b): White solid (21.5 mg, 63% yield), mp 102–104 °C,R_f = 0.76 (5% ethyl acetate in petroleum ether, v/v); ^{1}H NMR ($CDCl_3$, 600 MHz) δ_H 9.44 (s, 1H), 9.38 (d, J = 8.4 Hz, 1H), 8.64 (s, 1H), 8.44 (d, J = 8.4 Hz, 1H), 8.08 (d, J = 8.4 Hz, 1H), 8.05 (d, J = 9 Hz, 1H), 7.99 (d, J = 7.8 Hz, 1H), 7.80–7.77 (m, 1H), 7.74–7.71 (m, 1H), 7.67 (dd, J = 1.8, 9 Hz, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ_C 151.3, 141.9, 137.3, 133.9, 133.5, 131.9, 130.2, 128.3, 128.0, 127.8, 127.7, 127.2, 125.1, 124.8, 121.9, 120.0, 119.6; HRMS (ESI+) m/z calculated for $C_{17}H_{10}ClNNa$ $[M+Na]^+$ 286.0399, found 286.0402.

[1,3]Dioxolo[4′,5′:4,5]benzo[1,2-c]phenanthridine (19c): White solid (20.6 mg, 58% yield), mp 176–178 °C, R_f = 0.41 (5% ethyl acetate in petroleum ether, v/v); ^{1}H NMR ($CDCl_3$, 600 MHz) δ_H 9.42 (s, 1H), 8.75 (s, 1H), 8.67 (d, J = 8.4 Hz, 1H), 8.45 (d, J = 9.0 Hz, 1H), 8.13 (d, J = 7.8 Hz, 1H), 7.91–7.88 (m, 2H), 7.72 (t, J = 7.5 Hz, 1H), 7.30 (s, 1H), 6.15 (s, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ_C 151.7, 148.54, 148.52, 141.1, 132.9, 130.8, 130.2, 129.1, 128.7, 127.1, 126.9, 126.6, 122.1, 120.3, 118.4, 104.4, 102.3, 101.4; HRMS (ESI+) m/z calculated for $C_{18}H_{12}NO_2$ $[M+H]^+$ 274.0868, found 274.0857.

2-Fluorobenzo[c]phenanthridine (19d): White solid (25.4 mg, 79% yield), mp 142–143 °C, R_f = 0.55 (5% ethyl acetate in petroleum ether, v/v); ^{1}H NMR ($CDCl_3$, 600 MHz) δ_H 9.45 (s, 1H), 9.41–9.38 (m, 1H), 8.64 (d, J = 8.4 Hz, 1H), 8.55 (d, J = 9.0 Hz, 1H), 8.14 (d, J = 7.8 Hz, 1H), 7.94 (d, J = 9.0 Hz, 1H), 7.89 (td, J = 1.2, 7.5 Hz, 1H), 7.73 (t, J = 7.8 Hz, 1H), 7.59 (dd, J = 2.4, 9.6 Hz, 1H), 7.50 (td, J = 2.4, 8.7 Hz, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ_C 161.9 (d, J = 246 Hz), 152.4, 141.4, 134.4 (d, J = 10.5 Hz), 132.8, 131.0, 128.82, 128.78, 127.6 (d, J = 9 Hz), 127.2, 127.0 (d, J = 4.5 Hz), 126.7, 122.1, 121.3, 120.5, 116.4 (d, J = 24 Hz), 111.3 (d, J = 21 Hz); HRMS (ESI+) m/z calculated for $C_{17}H_{11}FN$ $[M+H]^+$ 248.0876, found 263.0879.

Formal Synthesis of *Arnottin I*

To a well stirred solution of $PdCl_2(CH_3CN)_2$ (22.0 mg, 0.085 mmol, 0.05 equiv.) in dry acetonitrile (3 mL) were added PPh_3 (89.1 mg, 0.34 mmol, 0.2 equiv.) and Cs_2CO_3 (422 mg, 1.3 mmol, 4.5 equiv.) successively. After stirring the reaction mixture at room temperature for 5 min, (6-iodo-2,3-dimethoxyphenyl)methanol **20**[30] (500 mg, 1.70 mmol, 1 equiv.) was added and the reaction was stirred at room temperature for 20 min. Next, 5-ethynyl-6-(2-methoxyvinyl)-benzo[*d*][1,3]dioxole **21**[14b] (377.7 mg, 1.87 mmol, 1.1 equiv.) was added and stirring at 80 °C was continued for another 6 hours until the completion of the reaction (TLC). The reaction mixture was quenched with water (5 mL) and extracted with ethyl acetate (3 × 10 mL). The combined organic extracts were washed with saturated brine (10 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The resulting crude was purified by silica-gel column chromatography (100-200 mesh)eluting with 35% petroleum ether-ethyl acetate (v/v) to produce the desired coupling product **22** in 68% yield.

***(2,3-Dimethoxy-6-((6-(2-methoxyvinyl)benzo [d][1,3]dioxol-5-yl)ethynyl)phenyl)methanol* (22)** (an inseparable mixture of *E*/*Z* isomers in the ratio 6:4): Brown gum (47.8 mg, 68% yield); R_f = 0.22 (50% ethyl acetate in petroleum ether, v/v); ^{1}H NMR ($CDCl_3$, 400 MHz) δ_H 7.62 (s), 7.26 (s), 7.24 (m), 7.00 (d, J = 12.8 Hz), 6.90–6.89 (m), 6.84–6.80 (m), 6.28 (d, J = 13.0 Hz), 6.17 (d, J = 6.8 Hz), 5.93–5.92 (m), 5.78 (d, J = 7.2 Hz), 4.92–4.90 (m), 3.88-3.87 (m), 3.76 (s), 3.71 (s); ^{13}C NMR ($CDCl_3$, 100 MHz) δ_C 153.1, 149.5, 148.5, 148.1, 147.9, 147.6, 145.6, 145.2, 135.9, 135.8, 133.5, 132.7, 128.6, 115.9, 114.2, 113.6, 112.1, 111.5, 111.2, 108.8, 103.8, 103.5, 103.2, 101.4, 91.3, 91.1, 90.0, 89.8, 61.5, 60.8, 59.3, 56.6, 55.9; HRMS (ESI+) m/z calculated for $C_{21}H_{21}O_6$ $[M+H]^+$ 369.1338 found 369.1340.

A mixture of $Pd(OAc)_2$bpy (3.8 mg, 0.01 mmol, 5 mol%), and D-CSA (125.3 mg, 0.54 mmol, 2 equiv.) in dry NMA (3 mL) was stirred at 90 °C for 5 min under argon atmosphere. Thereafter compound **22** (100 mg, 0.27 mmol, 1 equiv.) dissolved in NMA (1.5 mL) was added drop wise to the reaction mixture at the same temperature and the whole mixture was allowed to stir at 100 °C for few hours until the completion of the reaction (TLC). Next, the reaction mixture was neutralized by adjusting the pH (~7) through drop wise addition of 20% aqueous sodium bicarbonate solution and extracted with ethyl acetate (3 × 20 mL). The combined organic extracts were washed with saturated brine (10 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The resulting residue was purified through silica gel (100-200 mesh) column chromatography using 10–40% ethyl acetate-petroleum ether (v/v) as eluent to afford the desired product **23**.

1,2-Dimethoxy-13H-[1,3]dioxolo[4′,5′:4,5]benzo [1,2-h]benzo [c]chromene (23): Yellow solid (50.2 mg, 55% yield), mp 284–286 °C, R_f = 0.43 (10% ethyl acetate in petroleum ether, v/v); ^{1}H NMR ($CDCl_3$, 600 MHz) δ_H 7.61 (d, J = 8.4 Hz, 1H), 7.54 (s, 1H), 7.41 (d, J = 8.4 Hz, 1H), 7.32 (d, J = 8.7 Hz, 1H), 7.07 (s, 1H), 6.94 (d, J = 8.7 Hz, 1H), 6.04 (s, 2H), 6.36 (s, 2H), 3.91 (s, 3H), 3.90 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ_C 151.9, 148.8, 147.9, 147.5, 144.2, 131.1, 124.8, 124.3, 121.6, 120.5, 119.2, 117.6, 116.1, 111.7, 103.9, 101.2, 98.8, 63.6, 60.9, 55.8; HRMS

(ESI+) m/z calculated for $C_{20}H_{17}O_5$ $[M+H]^+$ 337.1076, found 337.1074.

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[23] a) CCDC 1901865 (**2 j**); b) CCDC 1801964 (**2′a**); c) CCDC 1901866 (**2′g**); d) CCDC 1901867 (**4′e**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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FULL PAPER

Palladium-Catalyzed Synthesis of 6*H*-Dibenzo[*c,h*]chromenes and 5,6-Dihydrobenzo[*c*]phenanthridines: Application to the Synthesis of Dibenzo[*c,h*]chromene-6-ones, Benzo[*c*]phenanthridines, and *Arnottin I*

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