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Synthesis of 5,6-dihydrobenz[*c*]acridines: a comparative study

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ABSTRACT

5,6-Dihydrobenz[*c*]acridines were synthesized by the reaction of 1-chloro-3,4-dihydro-2-naphthaldehyde with aromatic amines under three different conditions:

a. Thermolysis of 1-chlorovinyl-(*N*-aryl)imines prepared from 1-chloro-3,4-dihydro-2-naphthaldehyde.
b. Acid catalyzed cyclization of 1-(*N*-aryl)amino-3,4-dihydro-2-naphthaldehydes.
c. Thermolysis of *N*-arylenaminoimine hydrochlorides derived from 1-chloro-3,4-dihydro-2-naphthaldehyde in DMF medium.

All the three approaches exclusively yielded only 5,6-dihydrobenz[*c*]acridines and not the isomeric 7,8-dihydrobenzo[*k*]phenanthridines.
The structures of these products have been unambiguously established by detailed NMR spectral study and by independent synthesis as well as by single crystal XRD study.

1. Introduction

Quinolines and their derivatives are under constant investigation of the medicinal chemists in view of their profound range of biological activities viz., antimalarial,[1] anti-bacterial,[2] anti-asthmatic,[3] anti-hypertensive,[4] anti-inflammatory,[5] etc. The quinolone structural moiety is present in most of the anti-bacterials introduced in the recent past namely, Nalidixic acid,[6] Norfloxacin,[7] Ciprofloxacin,[8] Ofloxacin,[9] etc. In addition to their pharmaceutical applications, quinolines have also been employed in the study of bioorganic and bioorganometallic processes.[10]

The general approach for the synthesis of quinolines is based upon either Skraup,[11] Doebner–von Miller,[12] Combes[13] or Friedlaender[14] reaction. These reactions are still used for the manufacture of many quinoline derivatives and active pharmaceutical ingredients. Despite their versatility and simplicity, these reactions suffer from disadvantages like harsh conditions, difficult work-up procedures and lack of regioselectivity in the case of *meta*-substituted anilines. The recent progress in the synthesis of quinolines has been reviewed by Kouznetsov et al.[15]

In recent years, many publications have appeared on the chemistry of β-halo-α,β-unsaturated aldehydes[16] especially their use as synthons in the synthesis of condensed heterocycles like quinolines, benzacridines,[17] etc. Of the several methods available in the literature for the synthesis of quinoline derivatives, the one based on the thermal transformation of *N*-arylenaminoimine hydrochlorides is particularly useful for the preparation of 2-substituted, 2,3-disubstituted and 2,3-annulated quinolines. The first report of such a reaction was by Julia in 1950,[18] followed by that of Lloyd and Gagan.[19] The solution thermolysis of *N*-arylenaminoimine hydrochloride **2**, obtained by the reaction of β-chlorovinyl aldehyde **1** and arylamine as shown in Scheme 1, was found to be selective and led only to quinoline **3**. The formation of 2,3-disubstituted quinolines **3** in preference to the other regioisomeric 3,4-disubstituted quinolines **4** was rationalized by Lloyd et al. based on the conformational considerations and steric factors for the two modes of cyclization.

Since then, numerous reports have appeared in the literature on the thermolysis of *N*-arylenaminoiminium salts and this subject has been recently reviewed.[20] A facile synthesis of condensed benzopyrano[4,3-*b*]quinolines **7** by neat pyrolysis of *N*-arylenaminoimine hydrochlorides **6** derived from 4-chlorobenzopyran-3-carbaldehyde **5** was reported [21] (Scheme 2). The structures proposed for benzopyranoquinolines **7** were based on the earlier work of Jacquignon.[22]

An interesting and useful Buchwald amination of 1-chloro-3,4-dihydro-2-naphthaldehyde **9** with 2,5-dimethoxyanline yielding 1-(*N*-2,5-dimethoxy aryl)amino-3,4-dihydro-2-naphthaldehyde **11c** was described recently by Hesse and Kirsch.[23] The authors have reported that the reaction of 1-chloro-3,4-dihydro-2-naphthaldehyde

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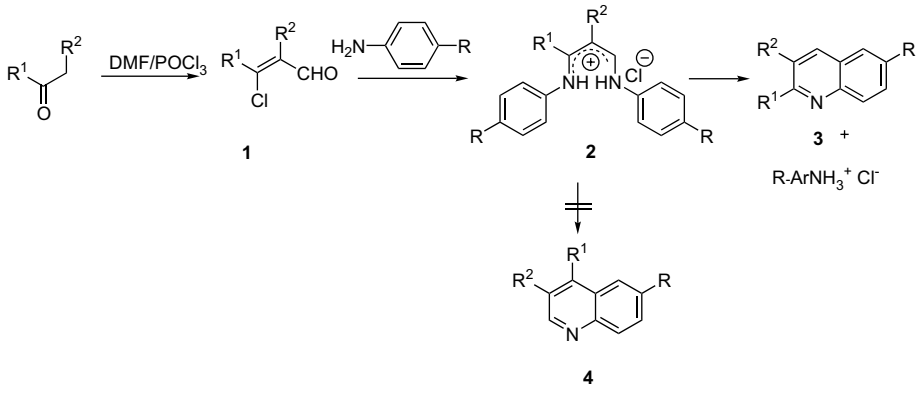
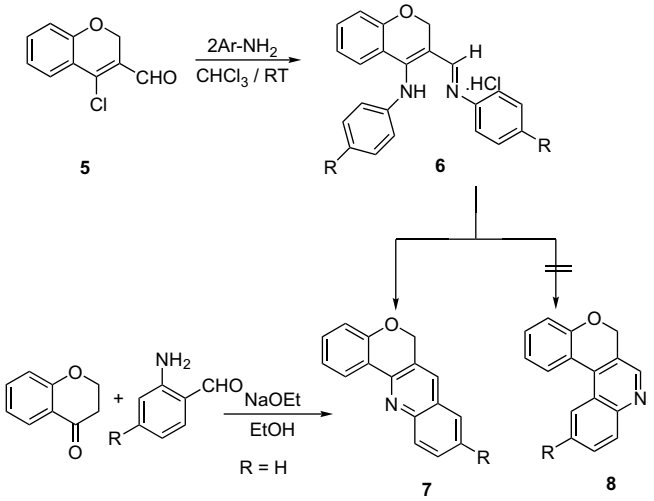


Scheme 1.



Scheme 2.

9 and 2,5-dimethoxyaniline with caesium carbonate in toluene (90 °C, 20 h, absence of the Pd catalyst) yielded hitherto unknown 7,8-dihydrobenz[*k*]phenanthridine **12c** (direct electrocyclization product) and dimethoxy 1-chloro-3,4-dihydro-2-naphthaldehyde imine **10c**, in a ratio of 3:1, respectively (Scheme 3). In addition, they observed the formation of the same cyclized product **12c** when the reaction was performed in isopropanol under reflux conditions for 4 h (Scheme 3). Surprisingly, there was no citation about the plausible alternate structure **13c**, arising by an alternate mode of cyclization which has a rich precedence in the literature.[17]

Literature survey for the synthesis of quinolines by thermal cyclization of the *N*-arylenaminoimine hydrochlorides and also for direct cyclization of 1-chloro-3,4-dihydro-2-naphthaldehyde[17] with anilines revealed that the C2 carbon of the quinoline formed stems from the β carbon of the β-chlorovinylaldehyde and not from the aldehydic carbon as one would normally expect out of six-electron cyclization. No exception to this mode of cyclization has been recorded so far. In line with this observation, thermal cyclization of the *N*-arylenaminoimines hydrochloride derived from 6-methoxytetralone would have furnished only 5,6-dihydrobenz[*c*]acridines **17** and not 7,8-dihydrobeno[*k*]phenanthridines **18**[24] (Scheme 4) as reported. In this regard, a study on the cyclization of 1-(*N*-2,5-dimethoxy aryl)amino-3,4-dihydro-2-naphthaldehyde **11c** would have shed some light in deducing the structure of this product.

In view of this conjecture, structure **12c** assigned for the cyclized product looked less probable and warranted a more thorough investigation by additional spectroscopic studies, which have been performed and delineated later in this paper.

Another publication that prompted us to disclose our own findings is a recent report on the chemoselective arylamination of 1-bromo-3,4-dihydro-2-naphthaldehyde[25] followed by acid catalyzed cyclization of 1-(*N*-aryl)amino-3,4-dihydro-2-naphthaldehydes **11**. With these background, we have conducted a detailed study on the thermal cyclization of *N*-arylenaminoimine hydrochloride salts **19**, 1-chlorovinyl-(*N*-aryl)imines **10** and also on acid catalyzed cyclization of 1-(*N*-aryl)amino-3,4-dihydro-2-naphthaldehydes **11**[20,26] (Scheme 5).

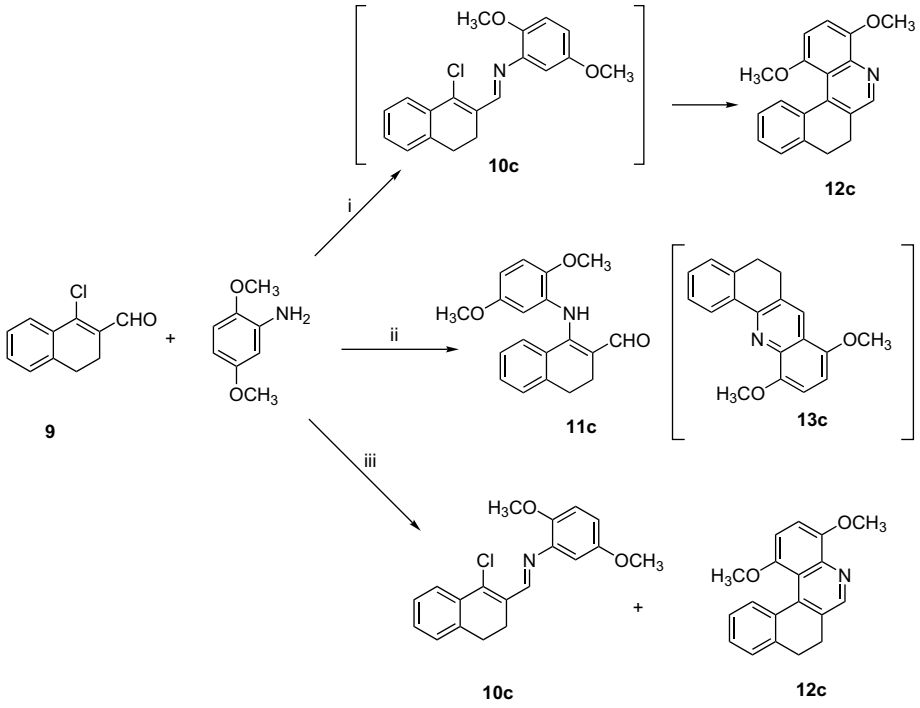
2. Results and discussion

2.1. Synthesis of 1-chlorovinyl-(*N*-aryl) imines and it's thermal cyclization

Normally, the β-chlorovinyl aldehydes are very reactive towards aromatic amines and they invariably lead to the formation of the *N*-arylenaminoimine hydrochlorides even at room temperature. We had earlier reported[27] a simple and facile synthesis of a number of 1-chlorovinyl-(*N*-aryl)imines of 4-chloro-3-formyl-2*H*[1]benzopyran and thiopyrans (Scheme 6) by reacting the carboxaldehydes, viz. 4-chlorobenzopyran-3-carboxaldehyde **5** and 4-chlorothiobenzopyran-3-caboxaldehyde **20**, with aromatic primary amines (dichloromethane, 0–5 °C, 2 h). Irradiation of **21** and **22** in methanol afforded benzopyrano [4,3-*b*]quinoline **7** and benzothiopyrano[4,3-*b*]quinoline **23**, respectively, in rather low yield (Scheme 7) while in the presence of a base no reaction was observed upon irradiation.

We had observed that under aforesaid conditions 1-chloro-3,4-dihydro-2-naphthaldehyde **9** (Scheme 7, Table 1) did not furnish the corresponding 1-chlorovinyl-(*N*-aryl)imines **10** but instead yielded *N*-arylenaminoimine hydrochlorides **19**. However, when the reaction was carried out in ethanol at 0–5 °C for 1–1.5 h it resulted in the selective formation of 1-chlorovinyl-(*N*-aryl)imines **10** in good yields.

It is worth mentioning here that there are only a very few reports available in the literature on the selective formation of 1-chlorovinyl-(*N*-aryl)imines by the reaction of 1-chloro-3,4-dihydro-2-naphthaldehyde **9** with naphthylamine.[28] However, the reaction of 1-chloro-3,4-dihydro-2-naphthaldehyde **9** with arylamines yielded only the corresponding *N*-arylenaminoimine hydrochlorides and not the 1-chlorovinyl-(*N*-aryl)imines.[29] A recent report[30] on the reaction of β-chloroacroleins with 2-aminophenol in DMF to yield the condensed quinolines clearly confirms the highly reactive nature of the aldehydes. It was proposed that the

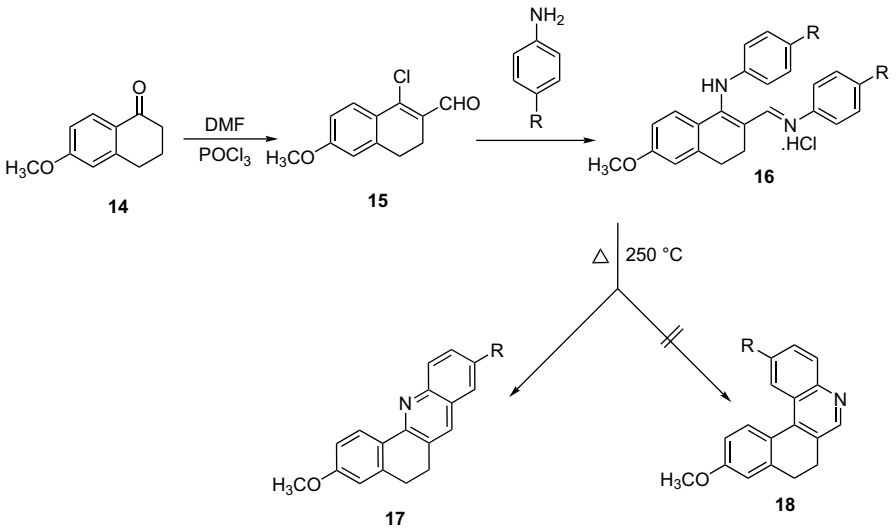


Scheme 3. Reagents and conditions: (i) 1 equiv **9**, 5 equiv 2,5-dimethoxyaniline, isopropanol, reflux, 4 h; (ii) 1 equiv **9**, 1 equiv 2,5-dimethoxyaniline, 3 mol % $Pd(OAc)_2$, 4 mol % BINAP, 1.3 equiv Cs_2CO_3, dry toluene, argon, 90 °C, 3 h; (iii) 1 equiv **9**, 1 equiv 2,5-dimethoxyaniline, 1.3 equiv Cs_2CO_3, dry toluene, argon, 90 °C, 20 h.

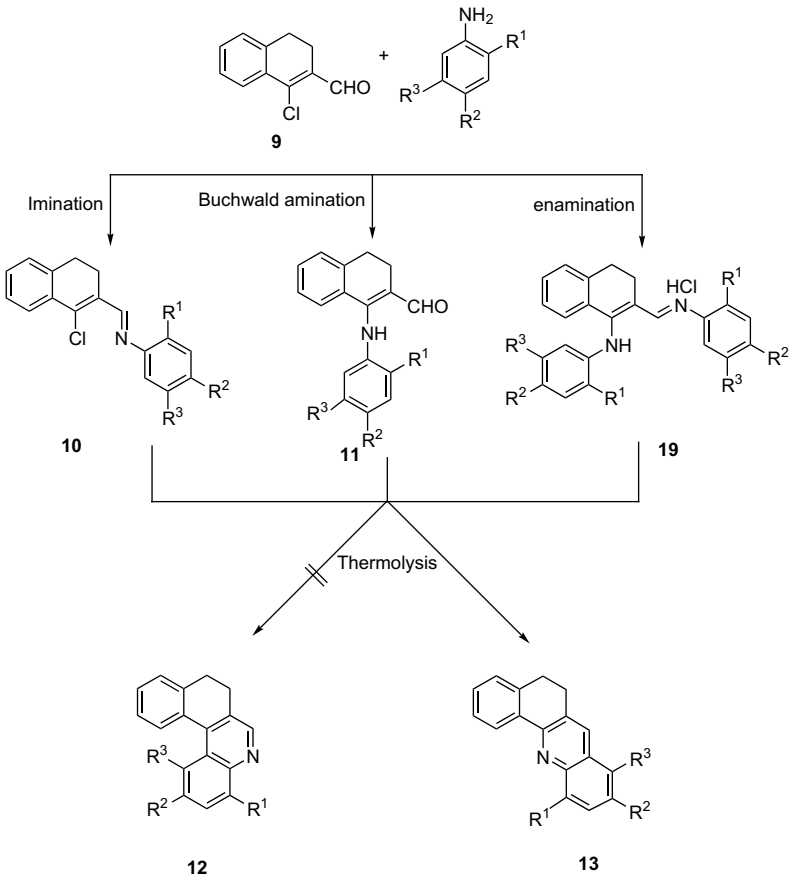
reactions proceed through the intermediacy of the 1-chlorovinyl-(*N*-aryl)imines. In this context, our observation on the selective reaction of arylamines with the β-chloroacroleins to form the 1-chlorovinyl-(*N*-aryl)imines in a few specified solvents/reaction conditions is worth mentioning.

The cyclization of 1-chlorovinyl-(*N*-aryl)imines **10** to the corresponding benz[*c*]acridines **13** has also been accomplished by heating in DMF at 140 °C for 1–1.5 h. Similarly, the reaction of 1-chloro-3,4-dihydro-2-naphthaldehyde **9** with 1-naphthylamine in ethanol afforded 1-chlorovinyl-(*N*-aryl)imines **24**, which on heating in DMF (140 °C, 4 h) yielded 5,6-dihydrobenz[*c*,*h*]acridine **25** as shown in Scheme 8.

We have studied the cyclization of 1-chlorovinyl-(*N*-aryl)imines **10** under different conditions viz. in refluxing DMF, in *N*-methylpyrrolidone at 140 °C and in refluxing chlorobenzene (Scheme 7). The conversion to 5,6-dihydrobenz[*c*]acridines **13** was accomplished under all these conditions except in refluxing chlorobenzene. It is interesting to note that a normal six-electron cyclization of this potential electrocyclic system to give 7,8-dihydrobenz[*k*]-phenanthridine **12** was not observed. The formation of the 5,6-dihydrobenz[*c*]acridine proceeds probably through the initial hydrolysis of the 1-chlorovinyl-(*N*-aryl)imines due to the inadvertent presence of moisture to generate a small amount of the aromatic primary amine, which in a subsequent reaction with the 1-chlorovinyl-(*N*-aryl)imines leads to the formation of the *N*-arylenaminoimine hydrochloride. The *N*-arylenaminoimine hydrochloride cyclizes to give the 5,6-dihydrobenz[*c*]acridine and 1 equiv of aromatic primary amine, which leads to the propagation of the cycle of reactions. When the progress of this reaction was monitored by TLC, it revealed the formation of the red coloured



Scheme 4.



	R^1	R^2	R^3
a	H	CH_3	H
b	H	OCH_3	H
c	OCH_3	H	OCH_3
d	H	Cl	H
e	H	H	H

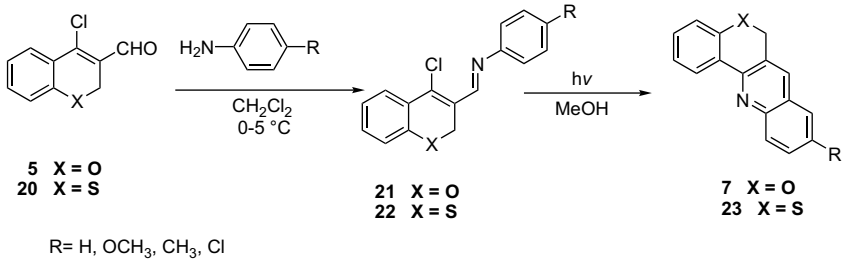
Scheme 5.

N-arylenaminoimine **19** as a transient intermediate and its subsequent conversion to the cyclized product. This transformation does not take place in DMF containing potassium carbonate.

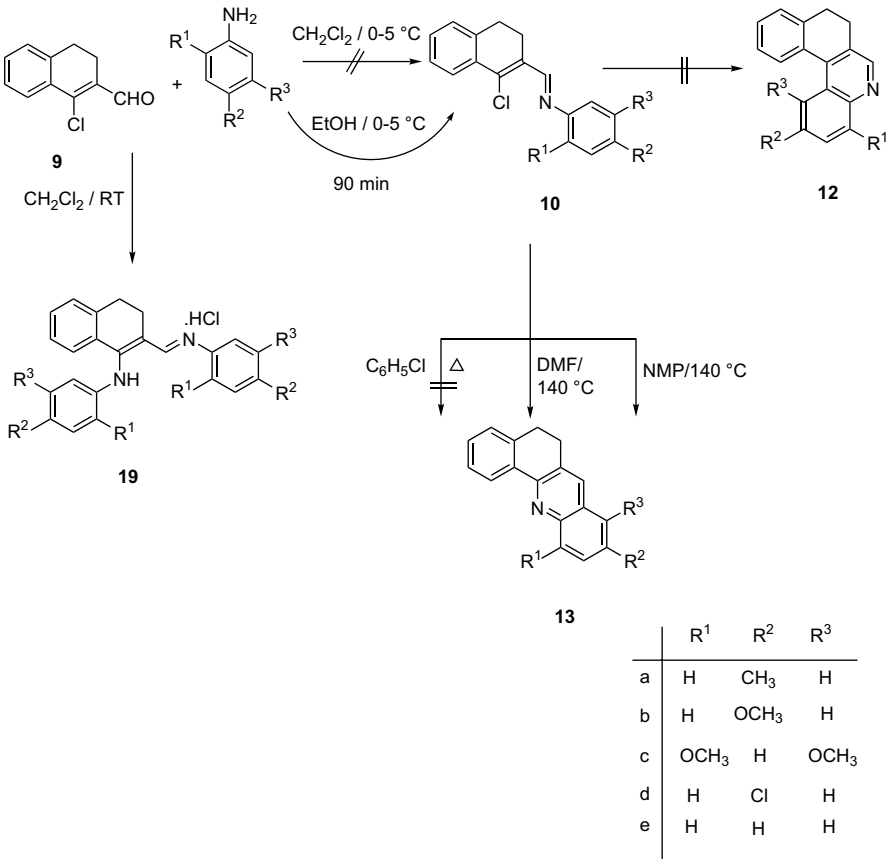
The structures of all these cyclized products have been unequivocally established as 5,6-dihydrobenz[*c*]acridines **13** (Table 2) as discussed below.

Although the reported[23] melting point and proton NMR spectral data of **12c** were identical to those of our product derived from the cyclization of **10c**, a detailed multinuclear analysis of this product by HH COSY, HSQC, HMBC and NOE clearly ruled out structure **12c** and strongly supported the alternative **13c** (Fig. 1). Of particular significance is the considerable deshielding of the H7 proton in the case of **13c** (δ 8.32) in comparison to those of **13a** and **13b** (δ 7.8).

Further support in favour of the 5,6-dihydrobenz[*c*]acridine structure was provided by the proton NMR spectrum of *N*-oxide **26**. The two doublets at δ 8.5 (H-1) and δ 8.0 (H-11) observed in the proton NMR spectrum of **13a** underwent a significant deshielding upon conversion to *N*-oxide **26** and appeared at δ 9.5 (H-1) and δ 8.5 (H-11), respectively (Scheme 9).



Scheme 6.



	R^1	R^2	R^3
a	H	CH_3	H
b	H	OCH_3	H
c	OCH_3	H	OCH_3
d	H	Cl	H
e	H	H	H

Scheme 7.

Table 1
Synthesis of 1-chlorovinyl-(*N*-aryl)imines **10a–e**

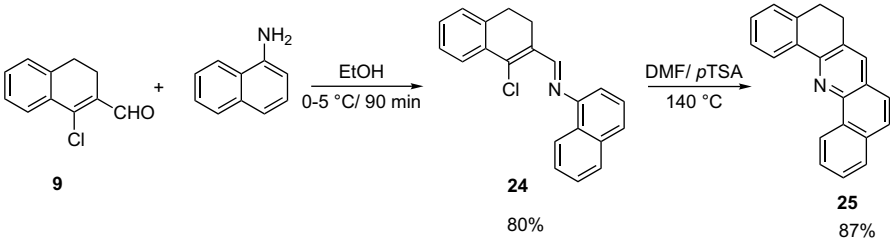
Entry	Product	R^1	R^2	R^3	Yield (%)	Mp (°C)
1	**10a**	H	CH_3	H	78	92–94
2	**10b**	H	OCH_3	H	75	82–84
3	**10c**	OCH_3	H	OCH_3	80	84–86
4	**10d**	H	Cl	H	90	140–142
5	**10e**	H	H	H	75	72–73

2.2. Synthesis of 1-(*N*-aryl)amino aldehydes and it's thermal conversion to 5,6-dihydrobenz[*c*]acridines

The assigned structure **13c** was further confirmed by an independent synthesis. Buchwald amination of 1-chloro-3,4-dihydro-2-naphthaldehyde **9** with aromatic amines in toluene as described by an earlier report[23] for 2,5-dimethoxyaniline (Cs_2CO_3, $Pd(OAc)_2$, *rac*-BINAP, 80 °C, 2 h) yielded the corresponding 1-arylamino-3,4-dihydro-2-naphthaldehydes **11** in moderate yields (Table 3, Scheme 10). Similarly, naphthylamino aldehyde **27** was prepared (Scheme 11). Heating these 1-(*N*-aryl)amino-3,4-dihydro-2-naphthaldehydes **11** in DMF containing catalytic amount of *p*-toluenesulfonic acid at 140 °C for 1 h furnished the corresponding 5,6-dihydrobenz[*c*]acridines **13** in moderate to good yields (Table 4). Similarly, cyclization of naphthylamino aldehyde **27** yielded dihydroacridine derivative **25** (Scheme 11).

Though the cyclization of the 1-(*N*-aryl)aminoaldehydes derived by the reaction of β-bromovinylaldehydes and arylamines is known,[25] it should be noted that the cyclization was carried out in trifluoroaceticacid as solvent for 10–12 h and the product was isolated by preparative thin layer chromatography. An independent synthesis of **13c** was reported[31] by reacting 2-amino-3,6-dimethoxybenzaldehyde with α-tetralone under basic conditions as shown in Scheme 12.

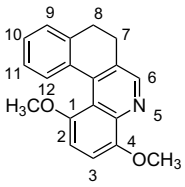
The melting point and proton NMR spectral data of products obtained from the thermal cyclization of **10c** and **11c** were identical with those reported,[31] further corroborating the assigned structure.



Scheme 8.

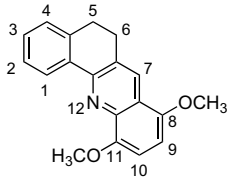
Table 2
Synthesis of 5,6-dihydrobenz[*c*]acridines **13a–e**

Entry	Product	R^1	R^2	R^3	Yield (%)	Mp (°C)
1	**13a**	H	CH_3	H	78	78–80
2	**13b**	H	OCH_3	H	90	112–114
3	**13c**	OCH_3	H	OCH_3	85	166–168
4	**13d**	H	Cl	H	90	100–102
5	**13e**	H	H	H	80	68–70



12c

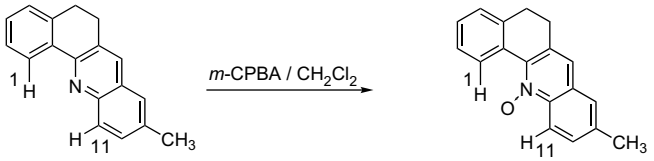
1,4-dimethoxy-7,8-dihydro[k]phenanthridine



13c

8,11-dimethoxy-5,6-dihydrobenz[c]acridine

Figure 1. Two plausible structures for the cyclization product of **10c**.



13a **26** 70%

Scheme 9.

Table 3
Synthesis of 1-(*N*-aryl)amino-2,3-dihydro-2-naphthaldehydes **11a–e**

Entry	Product	R^1	R^2	R^3	Yield (%)	Mp (°C)
1	**11a**	H	CH_3	H	70	82–84
2	**11b**	H	OCH_3	H	63	92–94
3	**11c**	OCH_3	H	OCH_3	65	112–114
4	**11d**	H	Cl	H	90	138–140
5	**11e**	H	H	H	55	126–128

The proposed structure was further confirmed by single crystal XRD study (Fig. 2).

Recently, we came across an interesting publication,[33] wherein it was observed that the Michael type addition of *p*-anisidine to the Knoevenagel product **28** furnished 5,6-dihydrobenz[*c*]acridine **13b** as shown in Scheme 13.

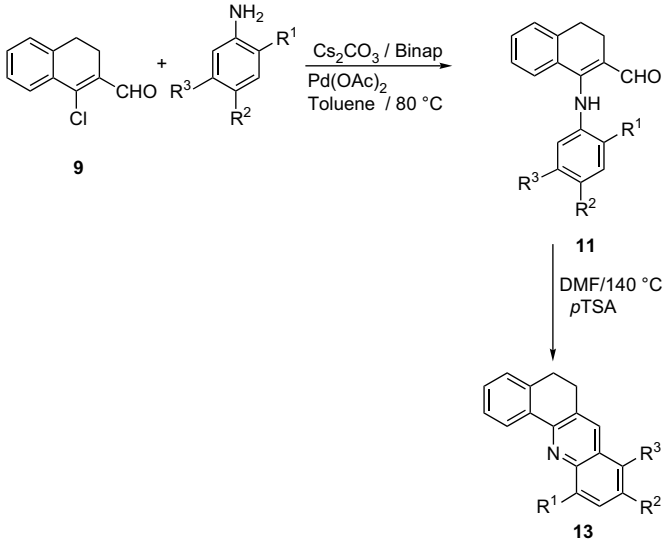
The assignment of this structure was based merely on the analytical data and proton NMR spectral data. Neither the reported melting point nor the proton NMR spectral data,[34] described in this paper agreed with those of ours. In view of this, we felt that this compound could be the hitherto unknown 7,8-dihydro-3-methoxybenzo[*k*]phenanthridine **12b** (Scheme 5, R_1=R_3=H; R_2=OCH_3). However, when we repeated this reaction following their procedure, we observed that the reaction did not go to completion even after long hours with 1 equiv of *p*-anisidine. Use of 2 equiv of *p*-anisidine led to complete conversion, furnishing a yellow solid that melted at 110–112 °C, contrary to the melting point of 248 °C reported by the authors. Also, we observed that the NMR spectral data differed considerably from those described in their paper. The melting point, proton NMR data and ^{13}C NMR spectral data of the product that we obtained were identical in all respects with those of **13b**.

2.3. Synthesis of symmetrical enaminoimines and their thermal studies

Adopting the procedure of an earlier published work[21] for an analogous system, reaction of 1-chloro-3,4-dihydro-2-naphthaldehyde **9** with a few aromatic amines (2 equiv) in $CHCl_3$ at room temperature for 3 h yielded the corresponding *N*-arylenaminoimine hydrochlorides **19** (Scheme 14 and Table 5). All these enaminoimines underwent a smooth cyclization when heated in DMF at 140 °C for 1–1.5 h. Quenching the reaction mixture in cold water directly yielded 5,6-dihydrobenz[*c*]acridines **13** in good yields (Table 6). The melting point and spectral data of the product in the case of the dimethoxy derivative **13c** were identical with those reported.[23] However, in the case of 1-naphthylamine the reaction with 1-chloro-3,4-dihydro-2-naphthaldehyde **9** in $CHCl_3$ yielded only the corresponding 1-chlorovinyl-(*N*-aryl)imines **25** and not *N*-arylenaminoimine hydrochloride **29** as shown in Scheme 15. This observation is similar to the one reported earlier.[28]

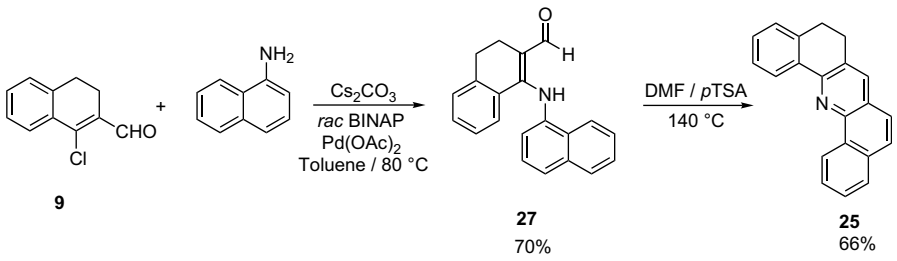
Most of the thermolysis of the *N*-arylenaminoimine hydrochlorides described in the literature have been carried out neat at very high temperatures ranging from 200 to 270 °C and involved an extensive work-up procedures. In contrast, our present method offers a simple and practical route for the synthesis of 5,6-dihydrobenz[*c*]acridines. It is worth mentioning here that the benzacridines are found to possess some carcinogenic properties whose chemistry has been reviewed.[35]

The cyclization of 1-chlorovinyl-(*N*-aryl)imines of 1-chloro-3,4-dihydro-2-naphthaldehyde provides a simple and alternate route for the synthesis of 5,6-dihydrobenz[*c*]acridines (Scheme 7). The main advantages of this method are shorter reaction time, easy work



9 **11** **13**

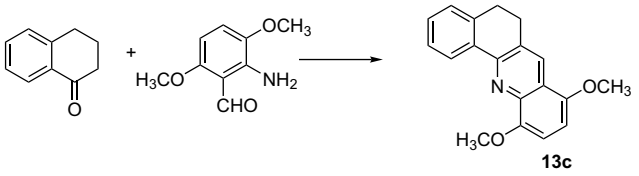
Scheme 10.



Scheme 11.

Table 4
Cyclization of 3,4-dihdyro-1-(*N*-arylamino)-2-naphthaldehydes to 5,6-dihydrobenz[*c*]acridines **13a–e**

Entry	Product	R^1	R^2	R^3	Yield (%)	Mp (°C)
1	**13a**	H	CH_3	H	65	78–80
2	**13b**	H	OCH_3	H	75	112–114
3	**13c**	OCH_3	H	OCH_3	62	166–168 (lit. 160–162)[31]
4	**13d**	H	Cl	H	72	100–102 (lit. 102)[32]
5	**13e**	H	H	H	75	68–70



Scheme 12.

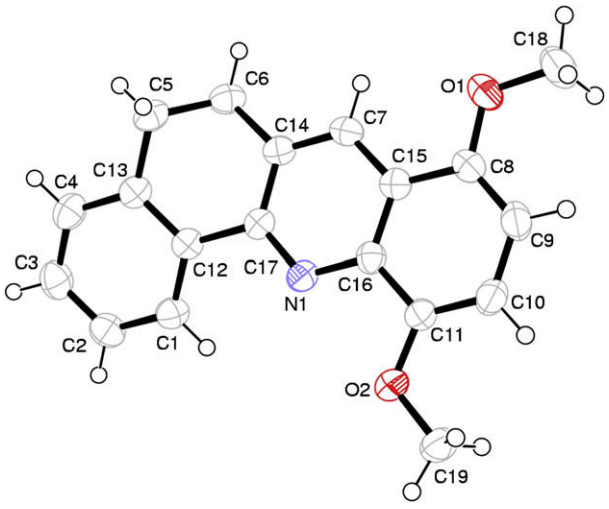
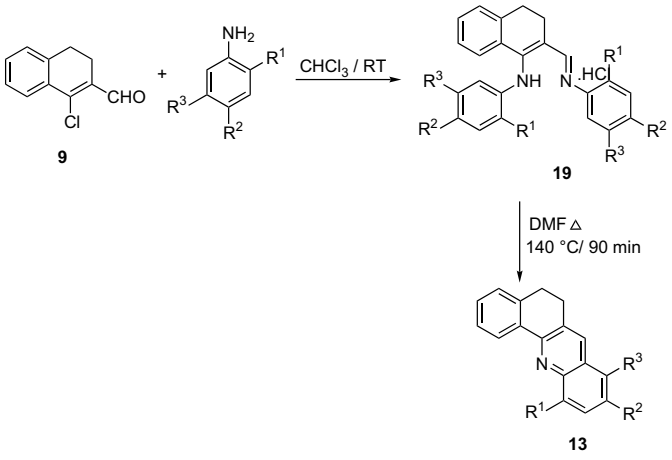


Figure 2. ORTEP diagram of compound **13c** with 50% probability.



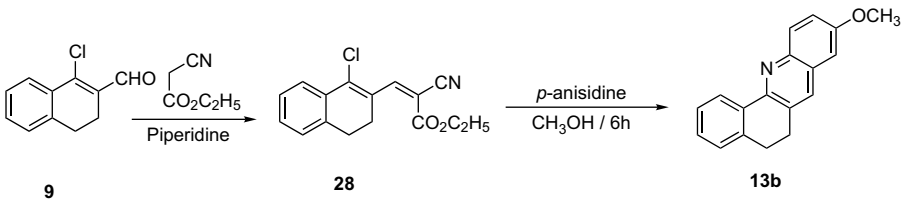
Scheme 14.

Table 5
Synthesis of *N*-arylenaminoimine hydrochlorides **19a–e**

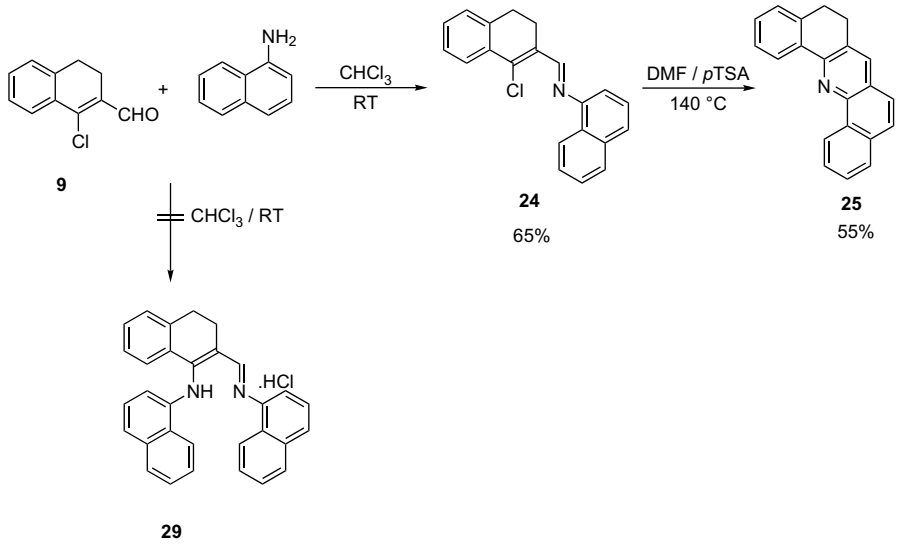
Entry	Product	R^1	R^2	R^3	Yield (%)	Mp (°C)
1	**19a**	H	CH_3	H	81	157–159
2	**19b**	H	OCH_3	H	68	147–149
3	**19c**	OCH_3	H	OCH_3	—	—
4	**19d**	H	Cl	H	80	168–169
5	**19e**	H	H	H	75	142–144

Table 6
Cyclization of *N*-arylenaminoimine hydrochlorides to 5,6-dihydrobenz[*c*]acridines **13a–e**

Entry	Product	R^1	R^2	R^3	Yield (%)	Mp (°C)
1	**13a**	H	CH_3	H	50	78–80
2	**13b**	H	OCH_3	H	60	112–114
3	**13c**	OCH_3	H	OCH_3	—	—
4	**13d**	H	Cl	H	75	100–102
5	**13e**	H	H	H	70	68–70



Scheme 13.



Scheme 15.

Table 7
A comparison of the three routes to the synthesis of 5,6-dihydrobenz[*c*]acridines

Entry	Product	Yield of 5,6-dihydro benzacridines (%)			Mp (°C)
		From 1-chlorovinyl-(*N*-aryl)imines	From 1-(*N*-aryl)-amino-2,3-dihydro-2-naphthaldehydes	From *N*-aryl enaminoimine hydrochlorides	
1	**13a**	78	65	50	78–80
2	**13b**	90	75	60	112–114
3	**13c**	85	62	—	166–168
4	**13d**	90	72	75	100–102
5	**13e**	80	75	70	68–70
6	**25**	87	66	—	152–154

up and isolation of the product. As 5,6-dihydrobenz[*c*]acridines are easily dehydrogenated to benz[*c*]acridines,[36,17c] the three routes that we have outlined in this work provide an easy access to a variety of benz[*c*]acridines. Comparison of the yields of 5,6-dihydrobenz[*c*]acridines by these three routes is shown in Table 7. Among these routes, the cyclization of 1-chlorovinyl-(*N*-aryl) imines using DMF appears to be the best in terms ease of preparation and yield. Also, it does not require the use of metal catalyst or the ligands.

3. Conclusion

To conclude the acid catalyzed solution thermolysis of the *N*-arylenaminoimine hydrochlorides, the 1-chlorovinyl-(*N*-aryl)-imines and the 1-(*N*-aryl)amino-3,4-dihydro-2-naphthaldehydes, all yielded the same 5,6-dihydrobenz[*c*]acridines in moderately good yields. The present methods offer practical and scalable routes for the synthesis of a wide variety of condensed quinolines. We had also attempted to bridge certain anomalies in the literature with sufficient evidences. Further work on this involving the benzopyrano, benzothiopyrano and coumarino compounds is ongoing.

4. Experimental

4.1. General methods

All reactions were carried out in oven-dried apparatus using dry solvents under anhydrous conditions. Commercial grade solvents were distilled and dried according to the literature procedures. Analytical TLC was performed on commercial plates coated with silica gel GF254 (0.25 mm). Silica gel (230–400 mesh) was used for column chromatography. The determined melting points are uncorrected. Yields refer to chromatographically and spectroscopically (^{1}H NMR) homogeneous materials, unless otherwise stated. ^{1}H NMR spectra were recorded on 300 MHz spectrometer. ^{13}C NMR spectra were recorded at 75 MHz spectrometer with complete proton decoupling and calibrated using residual undeuterated solvent as an internal reference. IR spectra were recorded on an FTIR spectrometer. High-resolution mass spectra (HRMS) were recorded on an electrospray mass spectrometer at Indian Institute of Technology Madras, Chennai 600 036, and Indian Institute of Sciences, Bangalore. Elemental analysis was done using Thermo Finnigan Flash EA 1112 elemental analyzer.

*4.1.1. Typical experimental procedure for 1-chlorovinyl-(N-aryl)imines **10a–e** and **24***

To a stirred solution of 1-chloro-3,4-dihydro-2-naphthaldehyde (1.0 g, 5.19 mmol) in ethanol (5 mL) containing catalytic amount of *p*-TSA at 0–5 °C was dropwise added a solution of arylamine (5.7 mmol) in ethanol (5 mL). The product was filtered after 1.5 h and recrystallized from hexane.

*4.1.2. Synthesis of (1-chloro-3,4-dihydro-naphthalen-2-ylmethylene)-p-tolylamine **10a***

Yellow solid (78% yield), mp 92–94 °C; R_f=0.69 (EtOAc/hexanes, 2:8); IR (KBr): 761, 818, 960, 1036, 1111, 1261, 1351, 1501, 1561, 1574, 1900, 2356, 2833, 2892, 2943, 3060 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.36 (s, 3H), 2.88–2.97 (m, 4H), 7.12–7.20 (m, 5H), 728–7.30 (m, 2H), 7.77–7.80 (m, 1H), 8.89 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.0, 23.7, 27.4, 121.0, 125.4, 126.7, 127.3, 129.5, 129.7, 132.7, 132.8, 136.2, 137.7, 138.2, 149.5, 157.6; HRMS *m*/*z* calculated for $C_{18}H_{16}ClN$ [M+H]: 282.1050, found: 282.1047.

*4.1.3. Synthesis of (1-chloro-3,4-dihydro-naphthalen-2-ylmethylene)-(4-methoxyphenyl)-amine **10b***

Yellow solid (75% yield), mp 82–83 °C; R_f=0.76 (EtOAc/hexanes, 2:8); IR (KBr): 758, 834, 1034, 1244, 1296, 1503, 1606, 1886, 2830, 2955, 3007 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.88–2.97 (m, 4H), 3.83 (s, 3H), 6.93 (d, 2H, *J*=8.8 Hz), 7.19–7.31 (m, 5H), 7.77–7.80 (m, 1H), 8.90 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 23.7, 27.4, 55.4, 114.3, 122.5, 125.3, 126.7, 127.3, 129.4, 132.7, 132.9, 137.2, 138.1, 144.9, 156.3, 158.5; HRMS *m*/*z* calculated for $C_{18}H_{16}ClNO$ [M+H]: 298.0914, found: 298.0913.

4.1.4. Synthesis of (1-chloro-3,4-dihydro-naphthalen-2-ylmethylene)-(2,5-dimethoxyphenyl)-amine ***10c***

Yellow solid (80% yield), mp 84–86 °C; R_f=0.65 (EtOAc/hexanes, 2:8); IR (KBr): 765, 841, 948, 964, 1042, 1110, 1220, 1261, 1299, 1339, 1446, 1501, 1583, 2361, 2830, 2905 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 2.88–3.01 (m, 4H), 3.81 (s, 3H), 3.85 (s, 3H), 6.63 (d, 1H, J=8.8 Hz), 6.73 (dd, 1H, J=2.8 and 8.6 Hz), 6.86 (d, 1H, J=8.8 Hz), 7.19–7.22 (m, 1H), 7.27–7.33 (m, 2H), 7.77–7.80 (m, 1H), 8.89 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 23.7, 27.3, 55.7, 56.5, 106.8, 111.1, 112.6, 125.5, 126.7, 127.4, 129.7, 132.7, 132.8, 138.3, 142.5, 146.6, 154.0, 159.7; HRMS m/z calculated for $C_{19}H_{18}ClNO_2$ [M+H]: 328.1104, found: 328.1101.

4.1.5. Synthesis of (1-chloro-3,4-dihydro-naphthalen-2-ylmethylene)-(4-chlorophenyl)-amine ***10d***

Yellow solid (90% yield); mp 140–142 °C; R_f=0.86 (EtOAc/hexanes, 2:8); IR (KBr): 765, 833, 961, 1087, 1160, 1182, 1243, 1262, 1350, 1452, 1575, 1593, 1896, 2348, 2834, 2896, 2948 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 2.92 (s, 4H), 7.13–7.16 (m, 2H), 7.21–7.23 (m, 1H), 7.28–7.34 (m, 3H), 7.36–7.38 (m, 1H), 7.78–7.81 (m, 1H) 8.85 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 23.5, 27.2, 122.3, 125.4, 126.7, 127.3, 129.1, 129.7, 131.6, 132.3, 132.6, 138.1, 138.6, 150.4, 158.6; HRMS m/z calculated for $C_{17}H_{13}Cl_2N$ [M+H]: 302.0503, found: 302.0501.

4.1.6. Synthesis of (1-chloro-3,4-dihydro-naphthalen-2-ylmethylene)-phenylamine ***10e***

Yellow solid (75% yield); mp 72–73 °C; R_f=0.69 (EtOAc/hexanes, 2:8); IR (KBr): 761, 823, 961, 1182, 1263, 1451, 1482, 1577, 1600, 2894 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 2.89–2.99 (m, 4H), 7.19–7.25 (m, 4H), 7.29–7.31 (m, 2H), 7.38 (t, 2H), 7.77–7.80 (m, 1H), 8.88 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 23.7, 27.4, 121.1, 125.5, 126.2, 126.8, 127.4, 129.1, 129.7, 132.6, 132.8, 138.1, 138.2, 152.2, 158.5; HRMS m/z calculated for $C_{17}H_{14}ClN$ [M+H]: 268.0893, found: 268.0897.

4.1.7. Synthesis of (1-chloro-3,4-dihydro-naphthalen-2-ylmethylene)-naphthalen-1-ylamine ***24***[28a]

Yellow solid (80% yield); mp 107–109 °C (lit. 110–111 °C); R_f=0.89 (EtOAc/hexanes, 2:8); IR (KBr): 765, 828, 960, 1077, 1149, 1265, 1393, 1435, 1559, 1592, 1958, 2375, 2927, 3014 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 2.95–3.00 (m, 2H), 3.09–3.14 (m, 2H), 7.08 (d, 1H, J=7.3 Hz), 7.30–7.33 (m, 2H), 7.44–7.53 (m, 3H), 7.72 (d, 1H, J=8.2 Hz), 7.80–7.86 (m, 2H), 8.31–8.34 (m, 1H), 8.98 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 23.8, 27.4, 112.8, 123.8, 125.5, 125.7, 126.0, 126.1, 126.4, 126.8, 127.4, 127.6, 128.9, 129.7, 132.8, 133.9, 138.2, 149.2, 158.3.

4.2. Typical experimental procedure for the preparation of 1-(*N*-aryl)amino-3,4-dihydro-2-naphthaldehydes 11a–e and 27

To a solution of 1-chloro-3,4-dihydro-2-naphthaldehyde (1.0 g, 5.19 mmol) in dry toluene (15 mL) were added Cs_2CO_3 (7.69 mmol), $Pd(OAc)_2$ (2.67 mmol) and racemic BINAP (0.16 mmol) under nitrogen atmosphere. The resultant mixture was heated to 80 °C and stirred for 1 h. A solution of aromatic amine (5.19 mmol) in dry toluene (5 mL) was then added dropwise to the above mixture. When the reaction was complete by TLC, the mixture was cooled to room temperature and filtered through Celite bed. The filtrate was then concentrated in vacuo to give the crude product, which was purified by column chromatography (Basic alumina, 20% EtOAC/Hexanes).

4.2.1. Synthesis of (1-p-tolylamino)-3,4-dihydro-naphthalene-2-carbaldehyde ***11a***

Yellow solid (70% yield); mp 82–84 °C; R_f=0.69 (EtOAc/hexanes, 2:8); IR (KBr): 743, 773, 814, 1006, 1143, 1178, 1231, 1322, 1336, 1388, 1437, 1511, 1554, 1588, 1605, 1625, 1886, 2730, 2803, 2916, 3024 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 2.33 (s, 3H), 2.48–2.54 (m, 2H), 2.82–2.87 (m, 2H), 6.79 (d, 2H, J=8.3 Hz), 6.94–7.00 (m, 3H), 7.18 (d, 1H, J=7.9 Hz), 7.22–7.26 (m, 2H), 9.40 (s, 1H), 11.85 (br, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.8, 23.5, 30.0, 109.7, 123.0, 125.6, 128.0, 128.8, 129.5, 130.0, 133.6, 138.7, 140.7, 153.1, 189.7. HRMS calculated for $C_{18}H_{17}NO$ [M+H]: 264.1388, found: 264.1381.

4.2.2. Synthesis of 1-(4-methoxy-phenylamino)-3,4-dihydro-naphthalene-2-carbaldehyde ***11b***

Red colour solid (63% yield); mp 92–94 °C; R_f=0.56 (EtOAc/hexanes, 2:8); ^1H NMR (300 MHz, $CDCl_3$): δ 2.48–2.55 (m, 2H), 2.81–2.86 (m, 2H), 3.76 (s, 3H), 6.73 (d, 2H, J=8.8 Hz), 6.85 (d, 2H, J=8.6 Hz), 6.92–6.98 (m, 1H), 7.15 (d, 1H, J=7.7 Hz), 7.22–7.26 (m, 2H), 9.38 (s, 1H), 11.13 (br, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 23.5, 30.2, 55.4, 109.0, 114.2, 124.7, 125.6, 128.0, 128.9, 130.0, 134.4, 140.9, 153.5, 156.5, 189.4; HRMS m/z calculated for $C_{18}H_{17}NO_2$ [M+H]: 280.1337, found: 280.1334.

4.2.3. Synthesis of 1-(2,5-methoxy-phenylamino)-3,4-dihydro-naphthalene-2-carbaldehyde ***11c***

Red crystalline solid (65% yield); mp 112–114 °C; R_f=0.48 (EtOAc/hexanes, 2:8); IR (KBr): 700, 718, 778, 853, 1005, 1086, 1141, 1234, 1391, 1442, 1490, 1555, 1602, 1619, 1936, 2832, 2940 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 2.51–2.55 (m, 2H), 2.81–2.86 (m, 2H), 3.54 (s, 3H), 3.78 (s, 3H), 6.26 (d, 1H, J=3.0 Hz), 6.50 (dd, 1H), 6.78 (d, 1H, J=6.0 Hz), 6.89–7.05 (m, 1H), 7.24–7.29 (m, 3H), 9.50 (s, 1H), 11.13 (br, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 23.2, 29.7, 55.6, 56.3, 108.1, 109.2, 112.1, 125.7, 127.8, 127.9, 129.4, 130.1, 131.7, 140.2, 145.1, 152.1, 153.3, 190.0.

4.2.4. Synthesis of 1-(4-chloro-phenylamino)-3,4-dihydro-naphthalene-2-carbaldehyde ***11d***

Yellow crystalline solid (90% yield); mp 138–140 °C; R_f=0.60 (EtOAc/hexanes, 2:8); IR (KBr): 774, 782, 848, 1002, 1023, 1143, 1168, 1219, 1252, 1319, 1367, 1440, 1511, 1555, 1577, 1600, 1631, 2829, 2924, 3412 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 2.51–2.55 (m, 2H), 2.82–2.87 (m, 2H), 6.81 (d, 2H, J=8.6 Hz), 6.97–7.04 (m, 1H), 7.14 (d, 3H, J=8.5 Hz), 7.27 (d, 2H, J=3.9 Hz), 9.44 (s, 1H), 11.67 (br, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 23.3, 29.7, 111.0, 123.8, 125.8, 128.1, 128.4, 128.5, 128.9, 130.3, 140.1, 140.4, 152.1, 190.6; HRMS m/z calculated for $C_{17}H_{14}ClNO$ [M+H]: 284.0842, found: 284.0846.

4.2.5. Synthesis of 1-(phenylamino)-3,4-dihydro-naphthalene-2-carbaldehyde ***11e***

Yellow solid (75% yield); mp 126–128 °C; R_f=0.68 (EtOAc/hexanes, 2:8); IR (KBr): 735, 778, 1188, 1256, 1385, 1416, 1491, 1556, 1580, 1605, 2831, 2922, 3025 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 2.57–2.68 (m, 2H), 2.75–2.79 (m, 2H), 6.67–6.83 (m, 1H), 6.93–6.97 (m, 2H), 7.10–7.15 (m, 3H), 7.17–7.20 (m, 3H), 9.36 (s, 1H), 11.67 (br, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): 23.4, 29.7, 110.4, 122.8, 123.8, 125.7, 128.0, 128.8, 128.9, 130.1, 140.5, 141.5, 152.6, 190.2; HRMS m/z calculated for $C_{17}H_{14}ClN$ [M+H]: 250.1232, found: 250.1236.

4.2.6. Synthesis of 1-(naphthalene-1-ylamino)-3,4-dihydro-naphthalene-2-carbaldehyde ***27***

Red solid (70% yield); mp 108–110 °C; R_f=0.69 (EtOAc/hexanes, 2:8); IR ($CHCl_3$): 791, 1016, 1145, 1175, 1241, 1267, 1358, 1386, 1557, 1581, 1602, 1624, 1672, 2838, 2927 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 2.57–2.61 (m, 2H), 2.88–2.93 (m, 2H), 6.77 (d, 1H, J=7.3 Hz), 6.83 (t, 1H, J=8.1 Hz), 6.99 (d, 1H, J=7.7 Hz), 7.16–7.27 (m, 3H), 7.52–7.62 (m, 3H), 7.87 (d, 1H, J=7.3 Hz), 8.39 (d, 1H, J=8.1 Hz), 9.50 (s, 1H), 12.18 (br, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 24.0, 30.4, 111.2, 121.8, 122.8, 125.0, 125.6, 126.1, 126.9, 128.4, 128.6, 128.8, 129.3, 130.5, 134.7, 138.0, 140.8, 154.5, 190.8; HRMS m/z calculated for $C_{21}H_{17}NO$ [M+H]: 300.1388, found: 300.1380.

4.3. Typical experimental procedure for the preparation of *N*-arylenaminoimine hydrochlorides 19a–e

A mixture of 1-chloro-3,4-dihydro-2-naphthaldehyde (1.0 g, 5.19 mmol) and arylamine (10.3 mol) in $CHCl_3$ (10 mL) was stirred at room temperature for 3.5 h. The precipitated red solid was filtered and recrystallizied in ethylacetate.

4.3.1. Synthesis of 1-[(p-methylphenyl)amino]-2-[((p-methyl phenyl)imino)methyl]-3,4-dihydro-naphthalene hydrochloride ***19a***

Red solid (81% yield); mp 170 °C; R_f=0.82 (EtOAc/hexanes, 2:8); IR (KBr): 756, 833, 1012, 1093, 1210, 1342, 1480, 1578, 1608, 1637, 2922, 3276, 3436 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$ and one drop DMSO-d_6): δ 2.03 (s, 3H), 2.31 (s, 3H), 2.79 (s, 4H), 6.95 (d, 2H, J=8.2 Hz), 7.01–7.10 (m, 5H), 7.21 (d, 1H, J=7.3 Hz), 7.30 (t, 2H), 7.48 (s, 1H), 7.74 (d, 2H, J=7.9 Hz), 8.99 (d, 1H, J=12.6 Hz), 11.49 (s, 1H), 11.94 (br, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.7, 20.8, 23.6, 28.9, 109.0, 119.0, 122.8, 126.0, 127.8, 128.4, 129.6, 129.9, 132.3, 134.9, 136.3, 136.6, 139.1, 143.6, 150.2, 161.2. Anal. Calcd for $C_{25}H_{25}ClN_2$: C, 77.20; H, 6.48; Cl, 9.12; N, 7.20. Found: C, 77.15; H, 6.41; Cl, 9.05; N, 7.39.

4.3.2. Synthesis of 1-[(p-methoxyphenyl)amino]-2-[((p-methoxy phenyl)imino)methyl]-3,4-dihydro-naphthalene hydrochloride ***19b***[17b]

Red solid (68% yield); mp 156 °C; R_f=0.52 (EtOAc/hexanes, 2:8); IR (KBr): 771, 813, 1020, 1093, 1265, 1431, 1546, 1615, 2853, 3144, 3350 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$ and one drop DMSO-d_6): δ 2.74–2.76 (m, 2H), 2.88–2.90 (m, 2H), 3.75 (s, 6H), 6.74–6.92 (m, 6H), 7.02–7.08 (m, 3H), 7.32–7.38 (m, 3H), 7.56 (d, 2H, J=8.6 Hz), 8.83 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 23.2, 28.6, 55.2, 108.8, 114.3, 114.4, 114.4, 119.1, 120.6, 123.9, 125.9, 128.3, 128.5, 128.7, 131.6, 135.1, 142.7, 151.2, 156.6, 157.8. Anal. Calcd for $C_{25}H_{25}ClN_2O_2$: C, 71.33; H, 5.99; N, 6.65. Found: C, 71.19; H, 6.03; N, 6.67.

4.3.3. Synthesis of 1-[(p-chlorophenyl)amino]-2-[((p-chlorophenyl)imino)methyl]-3,4-dihydro-naphthalene hydrochloride ***19d***

Red solid (80% yield); mp 186 °C; R_f=0.78 (EtOAc/hexanes, 2:8); IR (KBr): 721, 745, 779, 967, 967, 1088, 1197, 1234, 1338, 1489, 1538, 1601, 1628, 2847, 3035, 3257 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$ and one drop DMSO-d_6): δ 2.70–2.74 (m, 2H), 2.86–2.88 (m, 2H), 7.04 (t, 1H), 7.14 (d, 2H, J=8.7 Hz), 7.20–7.30 (m, 6H), 7.37 (m, 1H), 7.59 (s, 1H), 7.87 (d, 2H, J=8.5 Hz), 9.17 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 23.8, 28.8, 110.8, 120.7, 122.9, 123.9, 126.3, 127.1, 128.7, 129.2, 129.9, 130.1, 131.9, 133.0, 137.5, 140.3, 143.8, 151.1, 161.7. Anal. Calcd for $C_{23}H_{19}Cl_3N_2$: C, 64.28; H, 4.46; Cl, 24.75; N, 6.52. Found: C, 64.33; H, 4.52; Cl, 24.62; N, 6.51.

4.3.4. Synthesis of 1-phenylamino-2-(phenylimino)methyl-3,4-dihydro-naphthalene hydrochloride ***19e***

Red solid (75% yield); mp 148 °C; R_f=0.78 (EtOAc/hexanes, 2:8); IR (KBr): 685, 752, 777, 963, 1162, 1235, 1302, 1341, 1422, 1481, 1546, 1633, 2819, 3048, 3259 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 2.44–2.46 (m, 2H), 2.67–2.70 (m, 2H), 6.65 (t, 1H), 6.90 (t, 1H), 7.01 (t, 2H), 7.10–7.17 (m, 3H), 7.21–7.24 (m, 5H), 7.98 (d, 2H, J=8.1 Hz), 9.11 (d, 2H, J=14.6 Hz), 11.62 (s, 1H), 12.21 (d, 1H, J=14.6); ^{13}C NMR (75 MHz, $CDCl_3$): δ 24.9, 29.0, 111.8, 119.0, 122.4, 124.6, 125.5, 126.3, 127.3, 128.3, 128.8, 129.2, 130.4, 132.4, 138.3, 141.8, 144.0, 150.2, 160.8. Anal. Calcd for $C_{23}H_{21}ClN_2$: C, 76.55; H, 5.87; Cl, 9.82; N, 7.76. Found: C, 76.35; H, 5.84; Cl, 10.04; N, 7.76.

4.4. Typical experimental procedure for the preparation of 5,6-dihydrobenz[*c*]acridines 13a–e and 25

A stirred solution of 1-chlorovinyl-(*N*-aryl)imines or 1-(*N*-aryl)-amino-3,4-dihydro-2-naphthaldehydes or *N*-arylenaminoimine hydrochlorides (1.0 g, 1 equiv) in DMF (10 mL)/*p*-TSA was refluxed (140 °C) for 1–1.5 h. The reaction mixture was cooled to room temperature and poured over crushed ice. Filtering and drying yielded solids that were purified by column chromatography (10% EtOAc/hexane) to give the title compounds.

4.4.1. Synthesis of 9-methyl-5,6-dihydrobenz[c]acridine ***13a***

White crystalline solid; yield: 78% by imine route, 65% by aminoaldehyde route, 50% enaminoimine HCl route; mp 78–80 °C; R_f=0.72 (EtOAc/hexanes, 2:8); IR (KBr): 740, 763, 832, 917, 1018, 1040, 1140, 1255, 1291, 1375, 1442, 1496, 1599, 2361, 2848, 2938, 3024, 3420, 3735, 3839 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 2.33 (s, 3H), 2.95–3.00 (m, 2H), 3.06–3.10 (m, 2H), 7.25 (d, 1H, J=6.7 Hz), 7.31–7.45 (m, 3H), 7.48 (s, 1H), 7.79 (s, 1H), 8.01 (d, 1H, J=8.5 Hz), 8.55 (d, 1H, J=7.3 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.6, 28.4, 28.8, 125.8, 125.9, 127.2, 127.8, 129.0, 129.4, 130.5, 130.9, 133.0, 134.8, 135.8, 139.2, 146.2, 152.5; HRMS m/z calculated for $C_{18}H_{15}N$ [M+H]: 246.1282, found: 246.1285. Anal. Calcd for $C_{18}H_{15}N$: C, 88.13; H, 6.16; N, 5.71. Found: C, 88.16; H, 6.39; N, 5.90.

4.4.2. Synthesis of 9-methoxy-5,6-dihydrobenz[c]acridine ***13b***

White crystalline solid; yield: 90% by imine route, 75% by aminoaldehyde route, 60% by enaminoimine HCl route; mp 112–114 °C; R_f=0.66 (EtOAc/hexanes, 2:8); IR (KBr): 761, 828, 910, 1023, 1184, 1226, 1288, 1363, 1378, 1467, 1492, 1610, 2836, 2942, 3056 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 2.95–3.01 (m, 2H), 3.07–3.12 (m, 2H), 3.92 (s, 3H), 7.02 (d, 1H, J=2.1 Hz), 7.25–7.35 (m, 3H), 7.41 (t, 1H), 7.81 (s, 1H), 8.03 (d, 1H, J=9.2 Hz), 8.51 (d, 1H, J=7.3 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 28.4, 28.8, 55.5, 104.7, 121.1, 125.6, 127.2, 127.8, 128.8, 129.2, 130.8, 132.6, 134.8, 138.9, 143.6, 151.1, 157.6. HRMS m/z calculated for $C_{18}H_{15}NO$ [M+H]: 262.1232, found: 262.1237.

4.4.3. Synthesis of 8,11-dimethoxy-5,6-dihydrobenz[c]acridine ***13c***

Yellow crystalline solid; yield: 85% by imine route, 62% by aminoaldehyde route; mp 166–168 °C (lit. 160–162 °C); R_f=0.66 (EtOAc/hexanes, 2:8); IR (KBr): 721, 778, 794, 1099, 1259, 1384, 1459, 1602, 2835, 2931, 3737 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 2.97–3.02 (m, 2H), 3.11–3.16 (m, 2H), 3.96 (s, 3H), 4.06 (s, 3H), 6.71 (d, 1H, J=8.3 Hz), 6.89 (d, 1H, J=8.3 Hz), 7.25 (d, 1H, J=6.8 Hz), 7.32–7.42 (m, 2H), 8.32 (s, 1H), 8.62 (d, 1H, J=7.3 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 28.4, 28.9, 55.8, 56.4, 103.4, 106.7, 121.1, 126.4, 127.2, 127.8, 128.8, 129.6, 130.2, 134.7, 139.2, 139.9, 148.5, 149.7, 152.6; HRMS m/z calculated for $C_{19}H_{17}NO_2$ [M+H]: 292.1337, found: 292.1339.

4.4.4. X-ray crystallographic data of ***13c***

Structure was solved by direct methods (SIR92). Refinement was by full-matrix least-squares procedures on F^2 by using SHELXL-97. Crystal system: monoclinic, space group: $P2_1$, cell parameters: a=8.858(3), b=17.538(6), c=9.726(3) Å, α=90.00°, β=108.208(7)°, γ=90.00°, cell volume=1435.2(8) $Å^3$, and Z=4. The intensity data were collected on a Bruker SMART CCD area detector with graphite monochromated Mo Kα (λ=0.71073 Å) radiation. F(000)=616, μ=0.087 mm^{-1}. Total number ls parameters=201 for all 2519 data (CCDC no. 693163). Crystallographic data (excluding structure factors) for the structures in this paper have been deposited to the Cambridge Crystallographic Data Centre as supplementary publication. Copies of these data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033 or via e-mail: deposit@ccdc.cam.ac.uk or via www.ccdc.cam.ac.uk/conts/retrieving.html.

4.4.5. Synthesis of 9-chloro-5,6-dihydrobenz[c]acridine ***13d***

White crystalline solid; Yield: 90% by imine route, 72% by aminoaldehyde route, 75% enaminoimine HCl; mp 100–102 °C (lit. 102 °C); R_f=0.88 (EtOAc/hexanes, 2:8); IR (KBr): 725, 835, 914, 1075, 1136, 1289, 1342, 1394, 1484, 1598, 1934, 2848, 2940, 3028,

3047 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 2.98–3.03 (m, 2H), 3.10–3.14 (m, 2H), 7.28 (d, 1H, J=8.8 Hz), 7.35–7.45 (m, 2H), 7.57 (dd, 1H, J=2.3 and 9.0 Hz), 7.72 (d, 1H, J=2.1 Hz), 7.82 (s, 1H), 8.06 (d, 1H, J=9.0 Hz), 8.54 (dd, 1H, J=1.6 and 7.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 28.2, 29.2, 125.6, 126.0, 127.3, 128.0,128.4, 129.5, 129.9, 130.9, 131.6, 132.7, 134.3, 139.3, 145.9. 153.6.

4.4.6. Synthesis of 5,6-dihydrobenz[c]acridine ***13e***

White solid; Yield: 80% by imine route, 75% by aminoaldehyde route, 70% enaminoimine HCl; mp 68–70 °C; R_f=0.78 (EtOAc/hexanes, 2:8); IR (KBr): 737, 769, 861, 912, 951, 1098, 1125, 1290, 1409, 1431, 1456, 1493, 1553, 1598, 1814, 2949, 3036 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 2.95–3.00 (m, 2H), 3.06–3.11 (m, 2H), 7.22–7.25 (m, 1H), 7.35 (t, 1H), 7.38–7.47 (q, 2H), 7.63 (t, 1H), 7.71 (d, 1H, J= 7.9 Hz), 7.87 (s, 1H), 8.12 (d, 1H, J=8.4 Hz), 8.55 (d, 1H, J=8.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 28.4, 28.5, 126.0, 126.1, 126.9, 127.3, 127.9, 128.0, 128.6, 129.5, 129.7, 130.6, 133.7, 134.8, 139.5, 147.7, 153.4; HRMS m/z calculated for $C_{19}H_{17}NO_2$ [M+H]: 232.1127, found: 232.1122.

4.4.7. Synthesis of 5,6-dihydro-dibenz[c,h]acridine ***25***

White solid; yield: 87% by imine route, 66% by aminoaldehyde route; mp 154–156 °C (lit. 154–155 °C); R_f=0.75 (EtOAc/hexanes, 2:8); IR (KBr): 735, 748, 799, 819, 949, 1103, 1295, 1402, 1428, 1490, 1594, 1821, 2833, 2903, 2931, 3044; ^1H NMR (300 MHz, $CDCl_3$): δ 3.00–3.05 (m, 2H), 3.12–3.17 (m, 2H), 7.24–7.29 (m, 1H), 7.37 (t, 1H, J=7.2 Hz), 7.47 (t, 1H, J=7.3 Hz), 7.60–7.75 (m, 4H), 7.86–7.91 (m, 2H), 8.77 (d, 1H, J=7.5 Hz), 9.48 (d, 1H, J=8.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 28.3, 28.4, 124.4, 124.9, 125.6, 125.9, 126.7, 127.1, 127.2, 127.6, 127.7, 127.9, 129.4, 130.7, 131.8, 133.4, 134.0, 135.1, 139.0, 145.1, 151.5.

4.5. Typical experimental procedure of 9-methyl-5,6-dihydrobenz[*c*]acridine 12-oxide 26

A solution of the 9-methyl-5,6-dihydrobenz[*c*]acridine (500 mg, 2.04 mmol) and *meta*-chloroperbenzoic acid (3.06 mmol) in chloroform (2.5 mL) was stirred overnight at room temperature, and the solvent was removed. The crude product was purified by column chromatography (30% EtOAc/hexane) to give compound **26**.

Pale yellow solid (70% yield); mp 150–152 °C; R_f=0.32 (EtOAc/hexanes, 2:8); IR (KBr): 736, 749, 776, 820, 894, 1073, 1211, 1266, 1329, 1488, 1577, 1620, 2843, 2902, 2944, 3062 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 2.52 (s, 3H), 2.87–2.91 (m, 2H), 2.96–3.00 (m, 2H), 7.26–7.27 (m, 1H), 7.29–7.43 (m, 3H), 7.52 (d, 2H, J=9.6 Hz), 8.71 (d, 1H, J=8.6 Hz), 9.60 (dd, 1H, J=1.3 and 8.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.3, 29.3, 30.1, 120.0, 122.5, 126.1, 126.4, 127.4, 128.4, 128.5, 129.3, 130.0, 131.6, 133.6, 138.4, 139.9, 140.3, 140.4; HRMS m/z calculated for $C_{18}H_{15}NO$ [M+H]: 262.1232, found: 262.1234 (M+H). Anal. Calcd for $C_{18}H_{15}N$: C, 82.73; H, 5.79; N, 5.36; O, 6.12. Found: C, 82.85; H, 6.02; N, 5.57; O, 5.55.

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Supplementary data

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