Synthesis of linear dibenzo[1,8]naphthyridines using 2-chloro-4-methylquinolines

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DOI: http://dx.doi.org/10.3998/ark.5550190.0012.922

Abstract

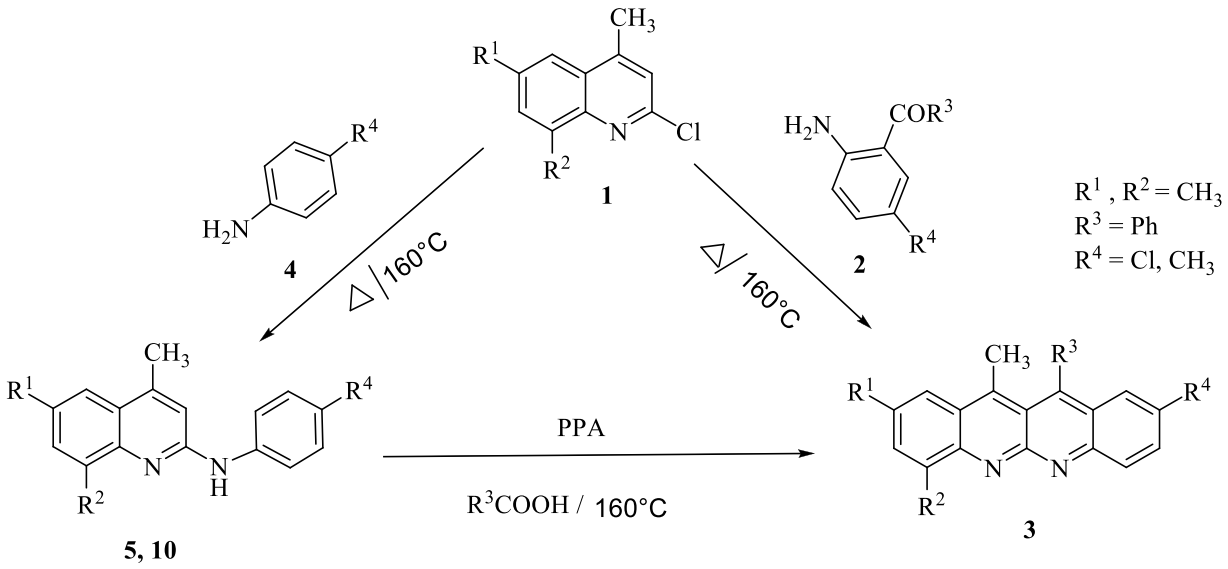
The attempted synthesis of linear dibenzonaphthyridines utilizing 2-chloro-4-methylquinolines leads to the formation of hitherto unknown compounds. The reaction of 2-chloro-4-methylquinoline with 2-amino-5-chlorobenzophenone afforded 6-chloro-10*H*-dibenzo[*b,g*]naphtho[1,2,3-*de*][1,8]naphthyridine. In an alternate way, anilinoquinolines were reacted with benzoic acid but yielded (dibenzo[*b,g*][1,8]naphthyridin-11(6*H*)-ylidene)-1-phenylethanone.

Keywords: 2-Chloro-4-methylquinolines, aminoketones, anilinoquinolines, novel dibenzonaphthyridines

Introduction

Quinoline and naphthyridine derivatives represent an important class of heterocycles as these ring systems occur in various natural products, especially in alkaloids and exhibit exceptionally broad spectrum of biological activities.[1-3] After the discovery of cinchona alkaloids as anti-malarial agents several anilinoquinolines were also established as synthetic antimalarials[4] and have been utilized as synthons in obtaining various fused heterocycles like indoloquinoline alkaloids.[5,6] Among the quinoline derivatives, pyrido fused quinolines (benzonaphthyridines) and quinoline fused quinolines (dibenzonaphthyridines) play an important role in living cells and in pharmaceuticals. Many reports represent the synthesis of linear[7,8] and angular dibenzonaphthridines[9-11] and only very few accomplish their construction through anilinoquinolines.[12,13] Marine sponges are proving to be productive sources of many interesting biologically active nitrogen-containing heterocyclic compounds, including a series of 1*H*-benzo[*de*][1,6]naphthyridine alkaloids.[14-16] Aaptamine *i.e.*, 8,9-dimethoxy-1*H*-benzo[*de*][1,6] naphthyridine was first isolated from marine sponge *Aaptos aaptos* and was found to possess

various biological activity like anti-neoplastic activity, cancer cell growth inhibitory activity[17] and recently found to activate p21 promoter in a p53 independent manner.[18] Isoaaptamine (8-methoxy-1-methyl-1*H*-benzo[*de*][1,6]naphthyridin-9-ol), a novel benzo[*de*][1,6]naphthyridine alkaloid of the aaptamine class isolated from an Indonesian marine sponge[19] was also reported to possess various biological activities. A formal total synthesis of the marine alkaloid aaptamine[20] and the synthetic conversion of aaptamine to isoaaptamine and other aaptamine derivatives[21] were also carried out with multisteps since simple construction of benzo[*de*]naphthyridine core structure is quiet tedious. Our present investigation though aimed in the preparation of linear dibenzonaphthyridines from 2-chloro-4-methylquinolines (**1**) by two methods (**i**) condensation of **1** with 2-amino-5-chlorobenzophenone **2** in single step.(**ii**) condensation of **1** with aniline **4** followed by cyclisation using benzoic acid in presence of PPA as represented in Scheme 1, ended up in hitherto unknown naphthyridine derivatives which also includes dibenzo[*b,g*]naphtho[1,2,3-*de*][1,8]naphthyridine.

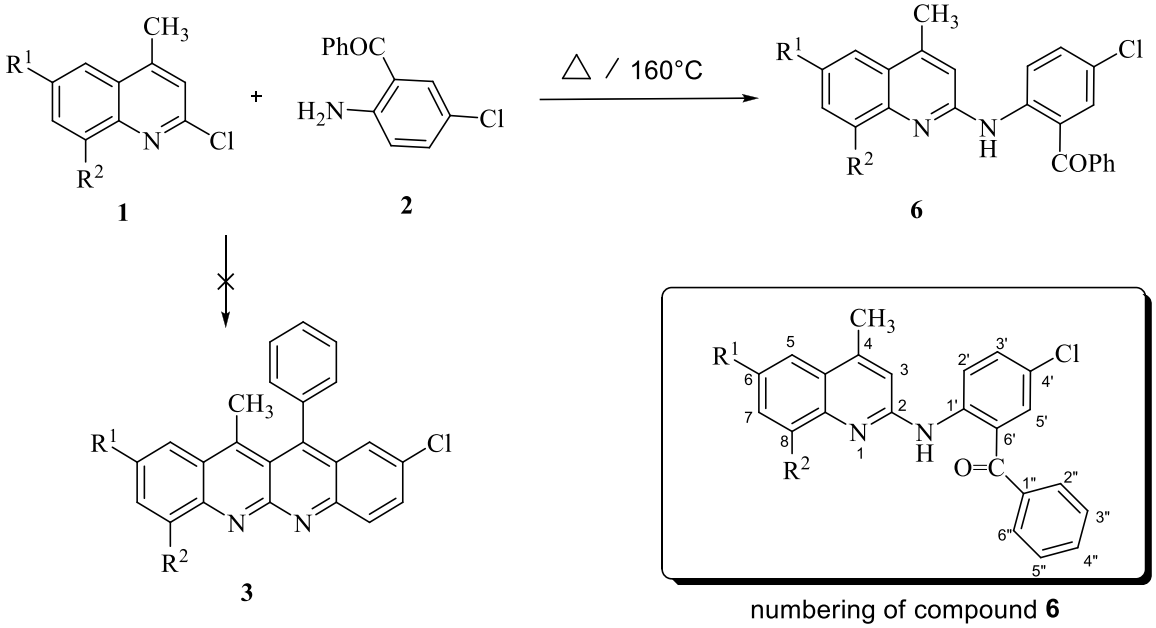


Scheme 1. Reaction sequences to achieve linear dibenzonaphthyridines.

Results and Discussion

In addition to our earlier work for the preparation of the angular dibenzonaphthyridines[22,23] from 4-chloro-2-methylquinolines and linear[24,25] and angular[26] dibenzonaphthyridines from 2,4-dichloroquinolines the objective of the present investigation was aimed in the preparation of some linear dibenzonaphthyridines from 2-chloro-4-methylquinolines. With regard to the earlier idea, the reaction of 2-chloro-4-methylquinolines **1a-c** with 2-amino-5-chlorobenzophenone **2** under neat condition at 160 °C (Scheme 2) afforded the products, namely 2[(2'-benzoyl-4'-chlorophenyl)amino]-4-methylquinolines **6a-c** and not the expected products **3** as observed in

earlier work.[22,23] In its ^{1}H NMR spectrum apart from the methyl groups in the aliphatic region all the aromatic protons resonated between δ 7.00-8.00 except for one proton doublet which was very much deshielded to~δ 9.50 and assigned to C6'-H (2D NMR pattern of similar compounds is discussed in our earlier work[24,25]). A broad singlet around δ 11.00 showed the presence of C2-NH (Hydrogen bonded). The conformations of the compounds **6a-c** is shown in Figure 1.



Scheme 2. Reaction of 2-chloro-4-methylquinoline **1** and 5-chloro-2-aminobenzophenone **2**.

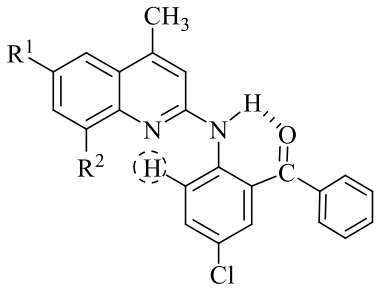
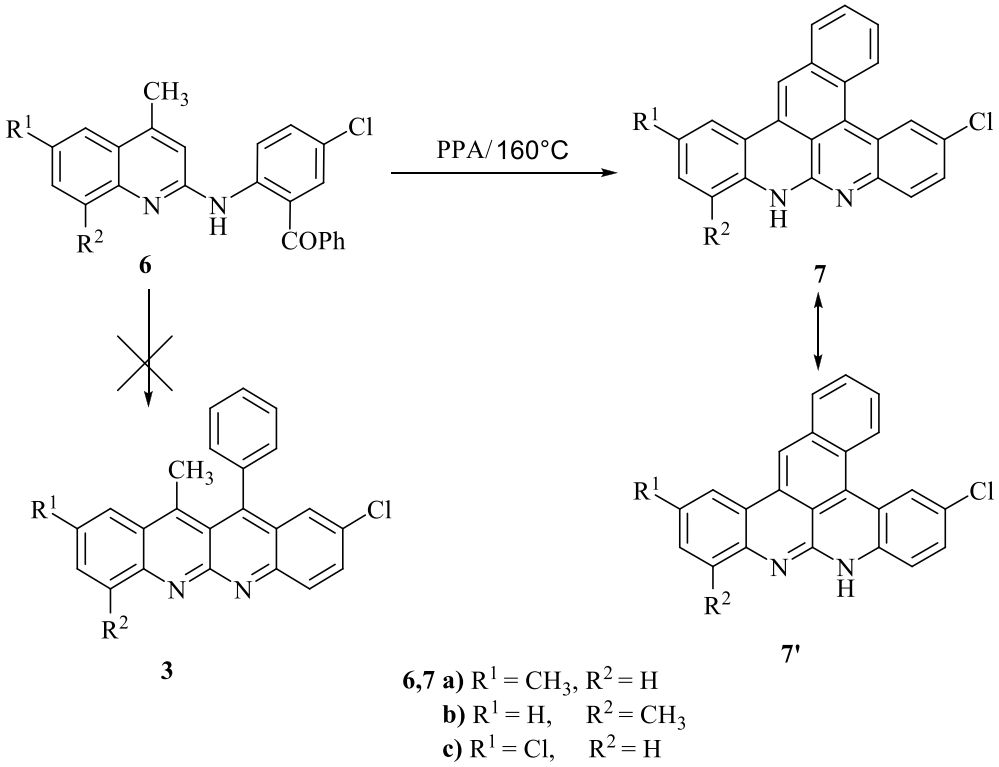


Figure 1. Conformations of 2[(2'-benzoyl-4'-chlorophenyl)amino]-4-methylquinolines **6a-c**.

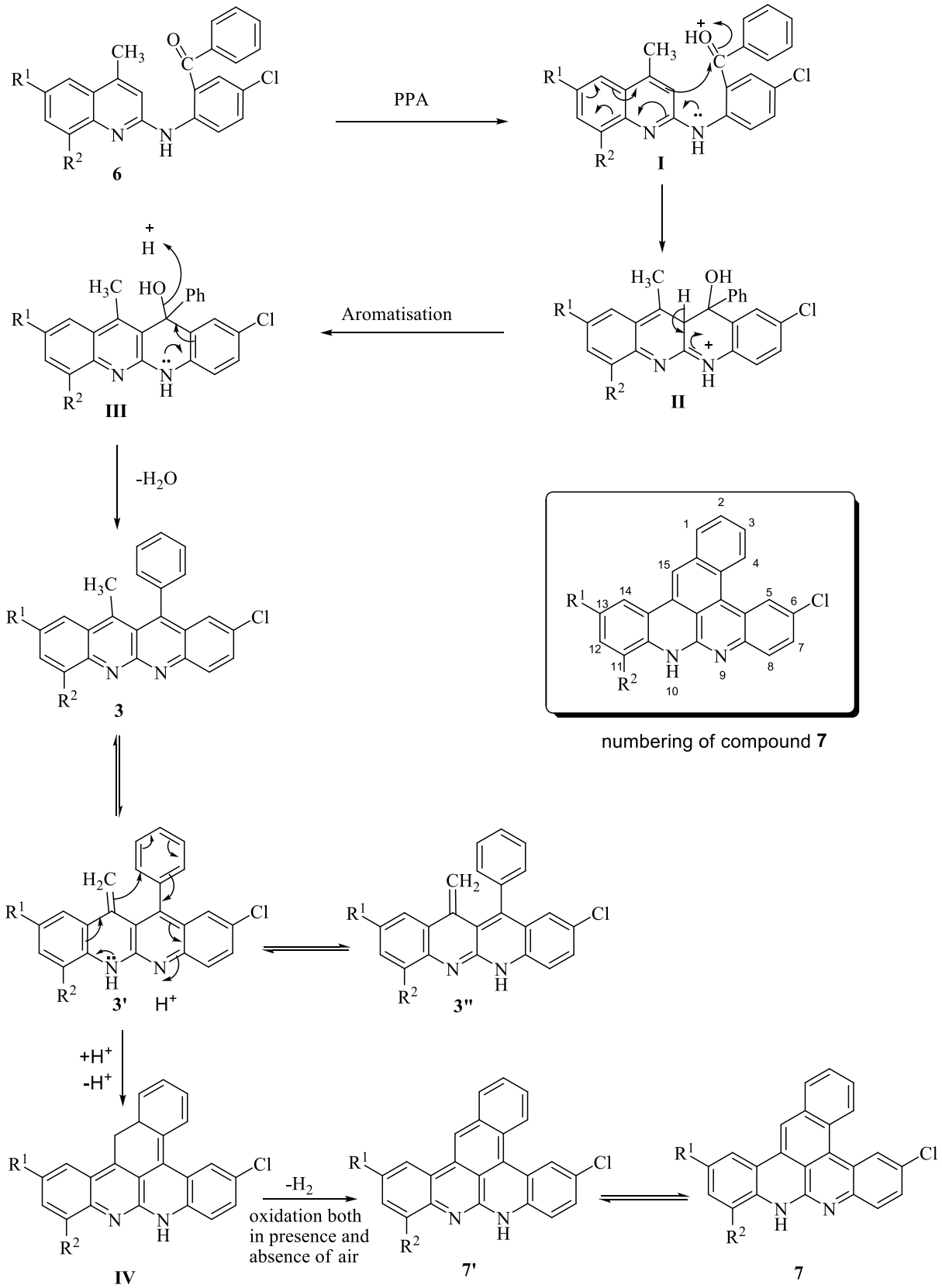
After obtaining the methylquinolines **6a-c** we aimed to cyclise them under acidic condition and hence 2[(2'-benzoyl-4'-chlorophenyl)amino]-4-methylquinolines **6a-c** were heated in presence of PPA at 160 °C for 5 hours to give the new products **7a-c**. Its ^{1}H NMR spectrum showed the absence of C3-H. The C7-and C9-CH_3 were observed around δ 2.50 for all the derivatives whereas the expected C11-CH_3 methyl group was absent. The appearance of a broad singlet at~δ 7.40 was due to N5-H/N6-H. Its ^{13}C NMR spectrum showed the presence of 24

carbons with the absence of C11-methyl carbon signal. The absence of methyl group and the presence of a NH group indicate that the methyl group might have involved further in reaction with the neighbouring phenyl ring. Finally the molecular ion peak for the compounds **7a,b** appeared at (*m/z)* 366 and *M+2* at 368 in its mass spectrum and the elemental analysis showed the molecular formula to be $C_{24}H_{15}ClN_2$ for its methyl derivative which confirmed that the compounds obtained were 6-chloro-10*H*-dibenzo[*b,g*]naphtho[1,2,3-*de*][1,8]naphthyridines **7a-c** (Scheme 3).



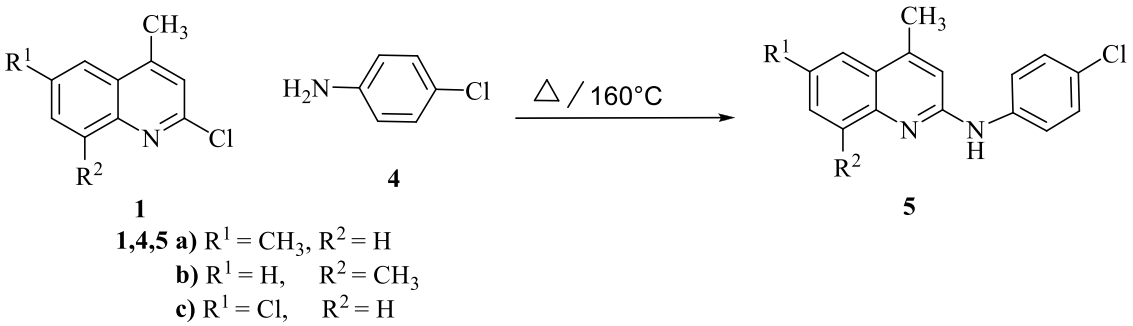
Scheme 3. Preparation of 6-chloro-10*H*-dibenzo[*b,g*]naphtho[1,2,3-*de*][1,8]naphthyridines **7a-c**.

The mechanism for the formation of the final compound **7** is proposed as follows in the Scheme 4. 2[(2'-Benzoyl-4'-chlorophenyl)amino]-4-methylquinoline **6** on intramolecular electrophilic substitution under the influence of H^+ donated by PPA afforded the intermediate **III** through the intermediates **I** and **II**. Then the intermediate **III** on the removal of H_2O molecule furnished the expected product **3**. The *in situ* formed product **3** on tautomerism gives the intermediate **3'** and **3''**. The intermediate **3'** on electrocyclic reaction *via* $=CH_2$ and neighbouring phenyl ring catalysed by protonation of the ring nitrogen afforded the intermediate **IV**. The intermediate **IV** on oxidation (either in presence of air or under N_2 atomosphere) furnished the final product 2-chloro-6,11-dihydro-naphthyl[3,2,1-*de*]dibenzo[*b,g*][1,8]naphthyridines **7** which is in equilibrium with its other tautomeric form **7'**.



Scheme 4. Proposed mechanism for the formation of **7** from **6**.

Now we chose an alternate way to diversify the target dibenzonaphthyridine where the anilinoquinolines were utilized as intermediates. Hence for the preparation of the anilinoquinoline, 2-chloro-4-methylquinolines **1a-c** were reacted with *p*-chloroaniline **4** under neat condition to afford 4-methyl-2(4'-chloro-phenylamino)quinolines **5a-c** (Scheme 5).

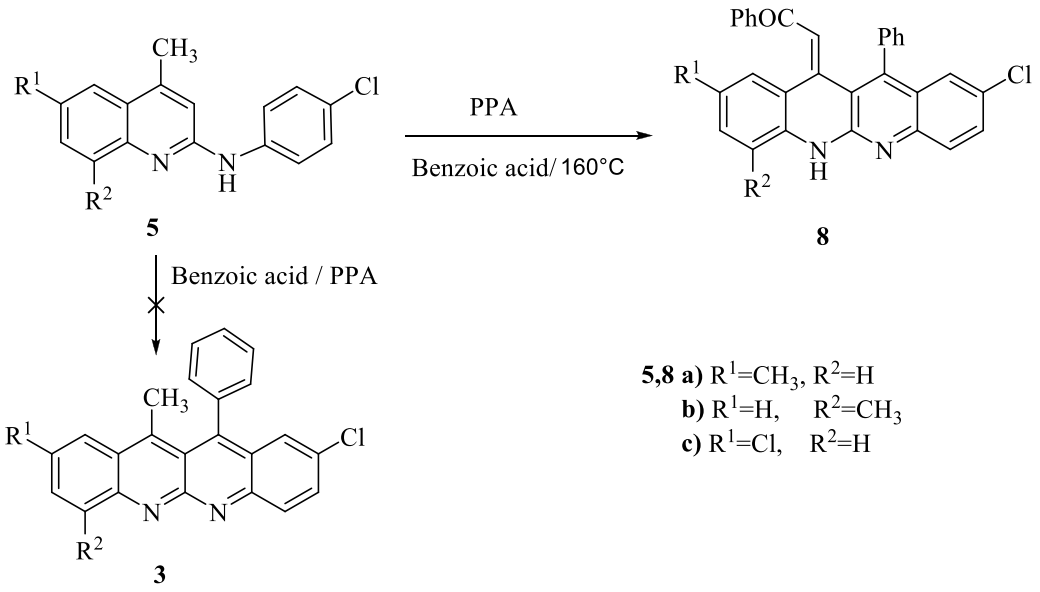


1 **4** **5**

1,4,5 a) $R^1 = CH_3$, $R^2 = H$
b) $R^1 = H$, $R^2 = CH_3$
c) $R^1 = Cl$, $R^2 = H$

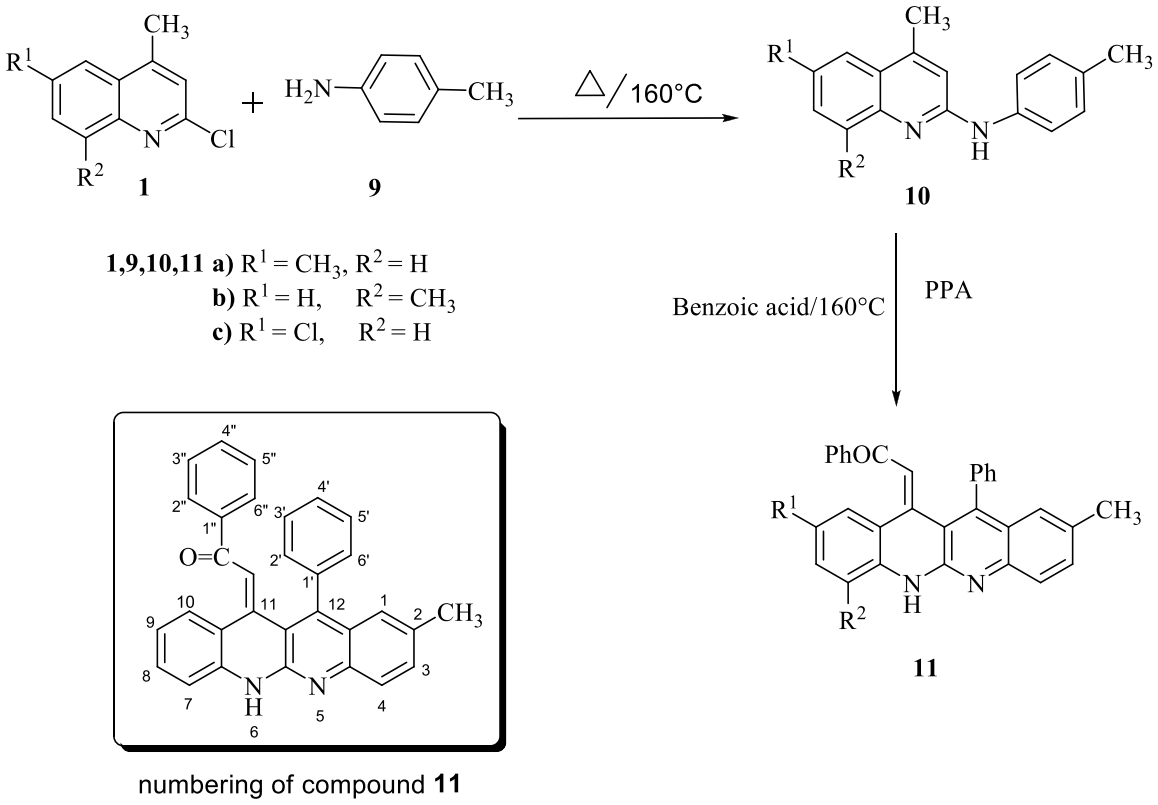
Scheme 5. Preparation of anilinoquinolines **5a-c**.

The anilinoquinolines **5a-c** thus obtained were treated with benzoic acid (slight excess) in presence of PPA at 150-155 °C. In the obtained products **8a-c**, besides the C7- and C9-CH_3 in the aliphatic region and aromatic protons, a broad singlet appeared around δ 9.00 due to N6-H. In this case also the appearance of a NH and the absence of C11-methyl protons suggest the formation of an unexpected product. Its ^{13}C NMR spectrum supported the presence of 31 carbons with the carbonyl carbon at~δ 185.4 which further supported by its IR spectrum. All these observations confirm the formation of the C11-benzoylated products. Finally its mass spectrum exhibited the molecular ion peak at (*m/z*) 472 and elemental analyses showed the molecular formula as $C_{31}H_{21}ClN_2O$ for its methyl derivative which confirmed the structure of the product formed as 2-(2-chloro-12-phenyldibenzo[*b,g*][1,8]naphthyridin-11(6*H*)-ylidene)-1-phenylethanones **8a-c** (Scheme 6).



Scheme 6. Reaction of anilinoquinolines **5a-c** with benzoic acid.

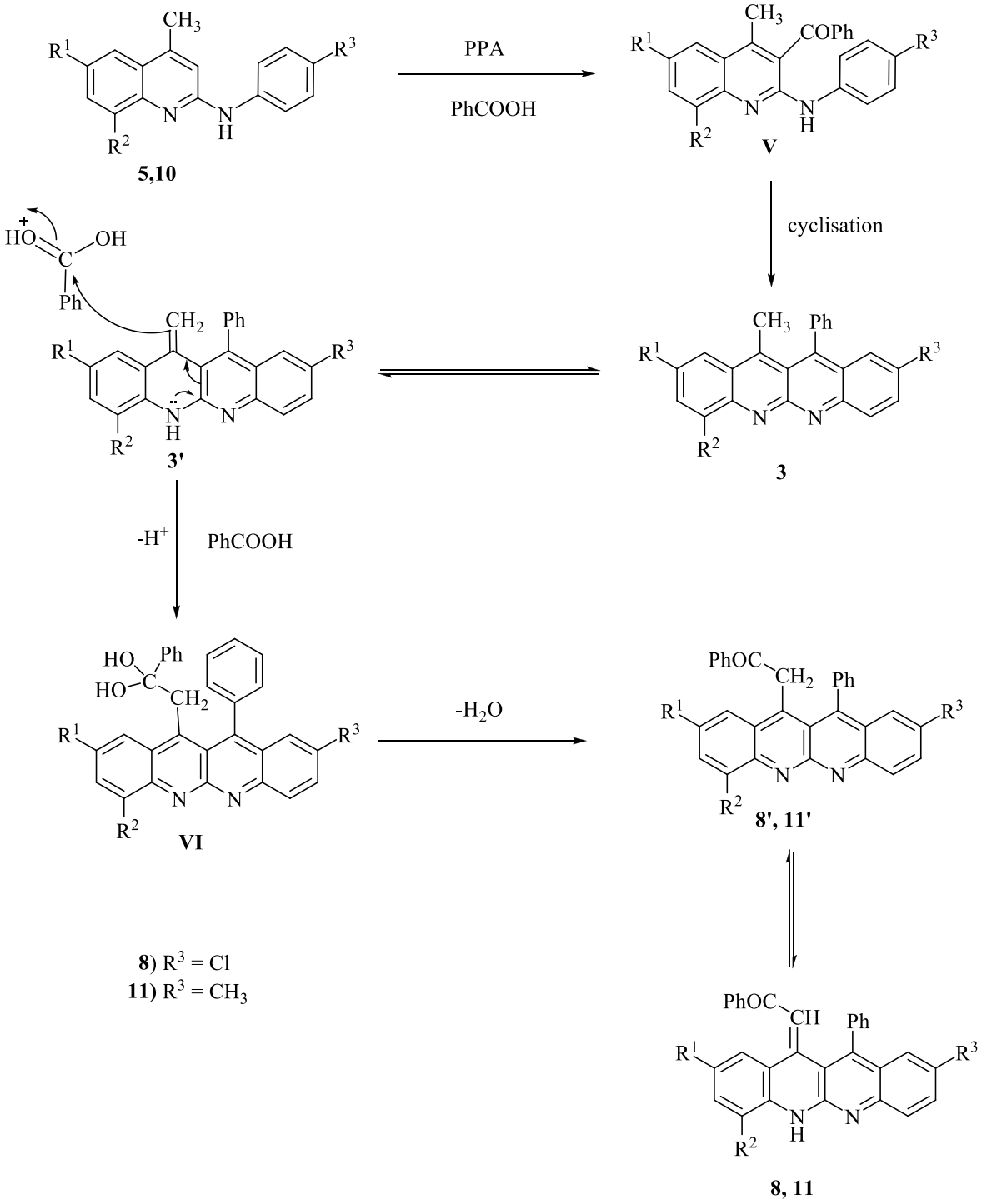
Similarly a set of reaction was performed in which **1a-c** were reacted with *p*-toluidine **9** to afford the corresponding anilinoquinolines **10a-c** and they were treated with benzoic acid to give 2-(2-methyl-12-phenyldibenzo[*b,g*][1,8]naphthyridin-11(6*H*)-ylidene)-1-phenylethanones **11a-c** (Scheme 7). In both the above cases for the formation of products **8** and **11** from the starting materials **5** and **10** respectively, the yield was poor (~ 20%) and the starting materials were recovered. When the same reaction was done with twice the quantity of benzoic acid no starting materials were recovered and the yield was good (~ 40%).



Scheme 7, Reaction of anilinoquinolines **10a-c** with benzoic acid.

The mechanism for the formation of the hitherto unknown compounds **8** and **11** is discussed in the Scheme 8. Benzoylation of anilinoquinolines **5,10** afforded **V** which on cyclisation yielded **3**. One of the tautomer **3'** reacts with benzoic acid to give intermediate **VI**

The intermediate **VI** on removal of H_2O molecule afforded the final dibenzonaphthyridines **8,11** through its tautomers **8',11'**.

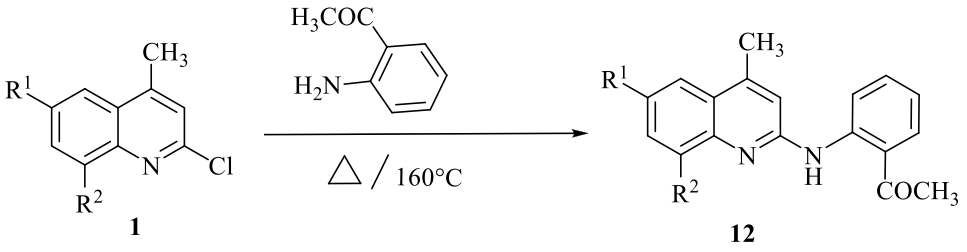


Scheme 8. Mechanism for the formation of **8,11**.

Various reaction conditions were optimized to isolate the possible intermediate **3**, but unsuccessful, perhaps the reason might be due to the less stability of the intermediate at the experimental condition. The similarity of the above couple of reactions conclude that after the

formation of the target cyclised dibenzonaphthyridines (*in situ*) the methyl group reacts further with the neighbouring phenyl ring or benzoic acid through its tautomeric form, thus ending up in the formation of hitherto unknown dibenzonaphthyridines. It is pertinent to mention here that anilinoquinolines do not react with benzoic acid unless PPA is present.

A similar set of reaction was aimed to perform with *o*-aminoacetophenone in order to get **12**. Hence 2-chloro-4-methylquinoline **1** and *o*-aminoacetophenone was reacted under neat condition at 160 °C to afford 2[(2'-acetylphenyl)amino]-4-methylquinoline **13** (Scheme 9).



Scheme 9. Reaction of 2-chloro-4-methylquinolines **1a-c** with *o*-aminoacetophenone.

As mentioned in the earlier case the peculiar deshielded C6'-H was assigned on the basis of the 2D NMR pattern of similar compound in our earlier work.[24,25] The conformation of the compound **12b** (similar to Figure 1) was confirmed by single crystal XRD studies. The ORTEP diagram of 2[(2'-acetylphenyl)amino]-4,8-dimethylquinoline **12b** is shown in Figure 2.

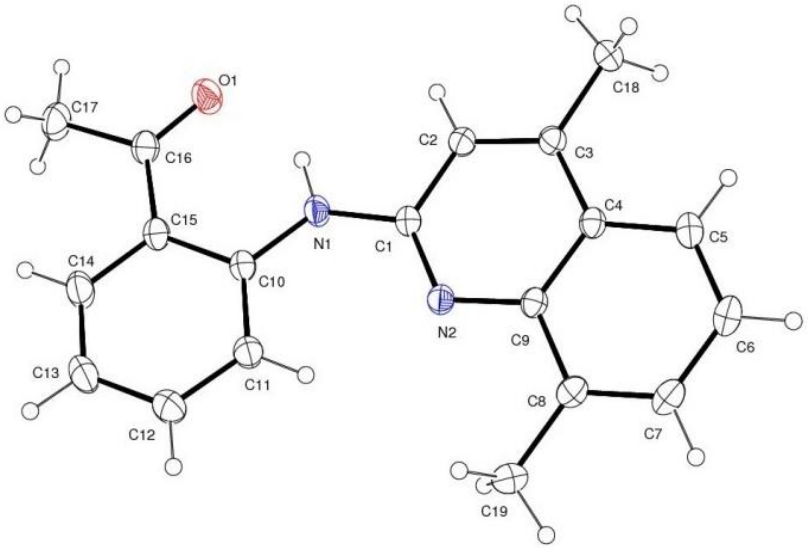


Figure 2. ORTEP diagram of 2[(2'-acetylphenyl)amino]-4,8-dimethylquinoline **12b.**

Conclusion

The attempted synthesis of linear dibenzonaphthyridines leads to the formation of novel compounds. The reaction of 2-chloro-4-methylquinolines **1** with amino ketones afforded the uncyclised **6** which further on acid catalysed cyclisation yielded hitherto unknown [*de*]dibenzonaphthyridines. In an alternate way to diversify the target compounds, **1** was converted to **5,10** and its further reaction with carboxylic acid led to the unknown dibenzonaphthyridin-ylidene-ones **8,11**. The reason for not realizing the target compounds **3** as expected might be the following reasons (i) less stability of the target compounds (ii) higher reactivity of C_{11}-methyl group of the compound **3**.

Experimental Section

General. Melting points (m.p) were determined on Mettler FP 51apparatus (Mettler Instruments, Switzerland) and are uncorrected. They are expressed in degree centigrade (°C). IR spectra were recorded on Schimadzu FTIR-8201PC spectrophotometer (Schimadzu, Japan) using KBr disc. ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker AMX 400 (400 MHz (^{1}H) and 100 MHz (^{13}C)) and AV 300 (300 MHz (^{1}H) and 75 MHz (^{13}C)) NMR spectrometer using tetramethylsilane (TMS) as an internal reference. The chemical shifts are expressed in parts per million (ppm). Mass spectra (MS), were recorded on AutoSpec EI+ shimadzu QP 2010 PLUS GC-MS mass spectrometer. Micro analyses were performed on a Vario EL III model CHNS analyser (Vario, Germany) at the Department of Chemistry, Bharathiar University. The purity of the products was tested by TLC with plates coated with silica gel-G with petroleum ether, ethyl acetate and methanol as developing solvents.

General procedure for the preparation of 2[(2'-benzoyl-4'-chlorophenyl)amino]-4-methylquinoline (6)

An appropriate 2-chloro-4-methylquinoline **1** (0.004 mol) was reacted with 2-amino-5-chlorobenzophenone **2** (0.004 mol) under neat condition at 160 °C for half an hour. The product was washed with water, adsorbed and purified using silica gel column chromatography and the product was eluted with petroleum ether ethyl acetate (98 2) mixture to get **6** which was then recrystallised using methanol.

2[(2'-Benzoyl-4'-chlorophenyl)amino]-4,6-dimethylquinoline (6a). Pale yellow prisms, Yield 65%, 1.004 g, mp 180-182 °C, IR (KBr) ν_{max} (cm^{-1}) 3397 (NH), 1639 (C=O), 1585, 1516, 1136. ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 2.58 (3H, s, C6-CH_3), 2.80 (3H,s, C4-CH_3), 6.88 (1H, s, C3-H), 7.21-7.78 (10H,m, C5, C7, C8, C3', C5', C2", C3", C4", C5", C6"-H), 9.48 (1H, d, C6'-H, J = 8.98 Hz), 11.12 (1H, b s, C2-NH), ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 20.7, 22.7, 112.4, 120.1, 120.7, 121.5, 123.3, 124.9, 126.0, 126.7, 127.8, 129.4, 130.0, 132.2, 133.2, 135.5, 137.2, 142.6, 145.5, 149.6, 152.0, 185.2, MS, (*m/z*) (%) 386 (M^+, 50), 357 (100), 343 (55), 322 (55), 281 (50), 245

(40), 77 (80), 66 (71), Anal. Calcd. for $C_{24}H_{19}ClN_2O$ C, 74.51, H, 4.95, N, 7.24. Found C, 74.99, H, 4.56, N, 7.15%.

2[(2'-Benzoyl-4'-chlorophenyl)amino]-4,8-dimethylquinoline (6b). Colourless needles, Yield 62%, 0.957 g, mp 174-176 °C, IR (KBr) ν_{max} (cm^{-1}) 3390 (NH), 1641 (C=O), 1595, 1515, 1150; ^1H NMR (400 MHz, $CDCl_3$) δ_H 2.69 (3H, s, C8-CH_3), 2.79 (3H, s, C4-CH_3), 6.83 (1H, s, C3-H), 7.24-7.73 (10H, m, C5, C6, C7, C3', C5', C2", C3", C4", C5", C6"-H), 9.51 (1H, d, C6'-H, *J* = 8.92 Hz), 11.01 (1H, b s, C2-NH), ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 19.8, 22.4, 114.6, 121.4 , 124.5, 124.3, 127.2, 128.8, 129.4, 129.7, 130.1, 130.9, 132.0, 132.6, 133.1, 137.1, 138.6, 142.6, 145.9, 150.1, 151.8, 183.5, MS, (*m/z*) (%) 388/386 (M^+, 15/50), 357 (100), 343 (38), 322 (60), 281 (42), 245 (38), 77 (95), 43 (86) Anal. Calcd. for $C_{24}H_{19}ClN_2O$ C, 74.51, H, 4.95, N, 7.24. Found C, 74.47, H, 5.00, N, 7.38%.

2[(2'-Benzoyl-4'-chlorophenyl)amino]-6-chloro-4-methylquinoline (6c). White solid, Yield 60%, 0.974 g, mp 186-188 °C, IR (KBr) ν_{max} (cm^{-1}) 3430 (NH), 1635 (C=O), 1580, 1521, 1139, ^1H NMR (400 MHz, $CDCl_3$) δ_H 2.68 (3H, s, C4-CH_3), 6.74 (1H, s, C3-H), 7.19-7.73 (10H, m, C5, C7, C8, C3', C5', C2", C3", C4", C5", C6"-H), 9.54 (1H, d, C6'-H, *J* = 9.00 Hz), 10.99 (1H, b s, C2-NH), ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 22.9, 114.3, 121.1, 121.4, 121.6, 124.1, 125.2, 126.2, 127.5, 128.2, 129.0, 131.2, 131.9, 133.5, 136.0, 137.4, 141.5, 144.2, 149.8, 150.2, 184.2, MS, (*m/z*) (%) 410/408/406 (M^+, 10/34/62), 378 (100), 371 (55), 322 (60), 281 (42), 196 (45), 76 (80), 43 (86), Anal. Calcd. for $C_{23}H_{16}Cl_2N_2O$ C, 67.82, H, 3.95, N, 6.87. Found C, 68.10. H, 4.07, N, 6.88%.

General procedure for the preparation of 6-chloro-10*H*-dibenzo[*b,g*]naphtho[1,2,3-*de*][1,8]naphthyridine (7)

2[(2'-Benzoyl-4'-chlorophenyl)amino]-4-methylquinoline **6** (0.002 mol) was heated in PPA (6 g of P_2O_5 and 3 mL H_3PO_4) at 160 °C for 5 hours. The reaction was monitored using TLC and after the completion of the reaction, the reaction mixture was poured into ice water, extracted using ethyl acetate and purified by column chromatography over silica gel and the product eluted with petroleum ether ethyl acetate (95 5) mixture to get **7** which was then recrystallised using methanol.

6-Chloro-13-methyl-10*H*-dibenzo[*b,g*]naphtho[1,2,3-*de*][1,8]naphthyridine (7a). Colourless prisms, Yield 45%, 0.329 g, mp 170-172 °C, IR (KBr) ν_{max} (cm^{-1}) 3405 (NH), 1591, 1521, 1148, ^1H NMR (400 MHz, $CDCl_3$) δ_H 2.44 (3H, s, C13-CH_3), 7.04-8.50 (10H, m, C1, C2, C3, C4, C5, C7, C8, C11, C12, C14-H), 7.41 (1H, b s, NH), 8.54 (1H, s, C15-H) ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 18.9, 122.3, 123.0, 123.4, 123.8, 123.9, 125.1, 125.6, 126.4, 126.9, 127.2, 127.8, 128.1, 128.7, 129.3, 129.8, 131.4, 131.8, 132.5, 132.8, 133.6, 143.8, 144.8, 154.0, MS,(*m/z*) (%) 368/366/ (M^+, 5/14), 352 (100), 326 (5), 315 (20), 264 (42), 176 (28), 158 (15), 76 (10) Anal. Calcd. for $C_{24}H_{15}ClN_2$ C, 78.51, H, 4.12. N, 7.63. Found C, 78.59, H, 4.21, N, 7.72%.

6-Chloro-11-methyl-10*H*-dibenzo[*b,g*]naphtho[1,2,3-*de*][1,8]naphthyridine (7b). Colourless needles, Yield 0.322 g, 44%, mp 168-170 °C, IR (KBr) ν_{max} (cm^{-1}) 3408 (NH), 1591, 1518, 1152, ^1H NMR (400 MHz, $CDCl_3$) δ_H 2.50 (3H, s, C11-CH_3), 7.05-8.38 (10H, m, C1, C2, C3,

C4, C5, C7, C8, C12, C13, C14-H), 7.36 (1H, b s, NH), 8.50 (1H, s, C15-H) ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 22.6, 122.0, 122.6, 122.9, 123.4, 123.9, 124.5, 125.4, 125.5, 126.0, 126.9, 127.6, 127.6, 128.8, 128.9, 129.8, 130.0, 130.7, 131.5, 131.8, 132.7, 142.8, 144.6, 153.5, MS, (*m/z*) (%) 368/366/ (M^+, 5/14), 352 (100), 315 (10), 293 (10), 289 (15), 266 (5), 161 (5), 134 (18), 76 (10), Anal. Calcd. for $C_{24}H_{15}ClN_2$ C, 78.51, H, 4.12, N, 7.63. Found C, 78.58, H, 4.06, N, 7.73%.

6,13-Dichloro-10*H*-dibenzo[*b,g*]naphtho[1,2,3-*de*][1,8]naphthyridine (7c). White solid, Yield 0.301 g, 39%, mp 173-175 °C, IR (KBr) ν_{max} (cm^{-1}) 3400 (NH), 1596, 1525, 1141, ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 7.04-8.41 (10H, m, C1, C2, C3, C4, C5, C7, C8, C11, C12, C14-H), 7.38 (1H, b s, NH) 8.48 (1H, s, C15-H) ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 122.4, 123.1, 123.2, 123.9, 124.3, 124.8, 125.7, 126.0, 126.5, 127.1, 127.6, 128.2, 128.6, 129.3, 129.9, 130.8, 131.4, 131.7, 132.3, 133.1, 142.6, 144.5, 153.6, MS, (*m/z*) (%) 388/386/384 (M^+, 5/14/32), 352 (100), 351 (10), 315 (5), 293 (10), 292 (8), 158 (15), 76 (10); Anal. Calcd. for $C_{23}H_{12}Cl_2N_2$ C, 71.33, H, 3.12, N, 7.23. Found C, 71.42, H, 3.03, N, 7.33%.

General procedure for the preparation of 4-methyl-2-(4'-chloro-phenylamino)quinoline (5)
A mixture of appropriate 2-chloro-4-methylquinoline **1** (0.010 mol) and *p*-chloroaniline **4** (0.010 mol) was heated under neat condition at 160 ºC for half an hour. The product obtained was washed with water, dried, purified by column chromatography over silica gel and eluted with ethyl acetate : methanol mixture (95 5) to get **5**. It was recrystallised using methanol.

4,6-Dimethyl-2-(4'-chloro-phenylamino)quinoline (5a). Pale yellow prisms, Yield 72%, 2.030 g, mp 120-122 ºC, (KBr) ν_{max} (cm^{-1}) 3436, 1588, 1520, 1135, ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 2.54 (3H, s, C6-CH_3), 2.78 (3H, s, C4-CH_3), 6.52 (1H, b s, C2-NH), 6.71 (1H, s, C3-H), 7.27 7.78 (7H, m, C5, C7, C8, C2', C3', C5', C6'-H), ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 20.7, 21.4, 113.5, 120.1, 120.9, 121.0, 122.2, 124.5, 126.2, 128.6, 129.2, 136.2, 144.1, 147.5, 153.8, MS, (*m/z*) (%) 282 (M^+, 100), 284 (M+2, 34), 281 (80), 265 (35), 247 (60), 246 (30), 220 (25), 90 (48), 77 (48), Anal. Calcd for $C_{17}H_{15}ClN_2$ C, 72.20, H, 5.34, N, 9.90. Found C, 72.10, H, 5.28, N, 9.73.

4,8-Dimethyl-2-(4'-chloro-phenylamino)quinoline (5b). Pale yellow prisms, Yield 75%, 2.115 g, mp 126-128 ºC, IR (KBr) ν_{max} (cm^{-1}) 3423, 1599, 1526, 1087, ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 2.60 (3H, s, C8-CH_3), 2.72 (3H, s, C4-CH_3), 6.56 (1H, b s, C2-NH), 6.69 (1H, s, C3-H), 7.21 7.76 (7H, m, C5, C6, C7, C2', C3', C5', C6'-H), ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 18.0, 21.7, 110.4, 120.6, 122.0, 122.5, 130.1, 131.0, 131.1, 132.7, 135.5, 137.5, 143.9, 148.5, 154.0; MS, (*m/z)* (%) 282(M^+, 100), 284 (M+2, 33), 28 (92), 265 (10), 247 (50), 246 (15), 140 (30), 84 (30), 77 (20), Anal. Calcd for $C_{17}H_{15}ClN_2$ C, 72.20, H, 5.34, N, 9.90. Found C, 72.13, H, 5.54, N, 9.32.

6-Chloro-4-methyl-2-(4'-chloro-phenylamino)quinoline (5c). Pale yellow spongy mass, Yield 70%, 2.114 g, mp 132-134 ºC, IR (KBr) ν_{max} (cm^{-1}) 3435, 1603, 1519, 1080, ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 2.83 (3H, s, C4-CH_3), 6.45 (1H, b s, C2-NH), 6.72 (1H, s, C3-H), 7.17-7.68 (7H, m, C5, C7, C8, C2', C3', C5', C6'-H), ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 21.7, 112.3, 120.2, 120.8,

121.5, 122.0, 123.3, 126.5, 127.8, 129.1, 138.0, 144.5, 147.7, 154.4; MS, (***m/z)*** (%) 306 (M+4, 32), 304 (M+2, 62), 302 (M^+, 100), 301 (85), 287 (70), 286 (30), 285 (15), 267 (61), 165 (45), 77 (42), Anal. Calcd for $C_{16}H_{12}Cl_2N_2$ C, 63.38, H, 3.98, N, 9.23. Found C, 63.13, H, 4.03, N, 9.67.

General procedure for the preparation of 2-(2-chloro-12-phenyldibenzo[*b,g*][1,8]naphthyridin-11(6*H*)-ylidene)-1-phenylethanone (8)

An appropriate mixture of 4'-chloro-4-methyl-2-(*N*-phenylamino)quinoline **5** (0.0010 mol) and benzoic acid (0.0011 mol) was added to polyphosphoric acid (3 g of P_2O_5 in 1.5 mL of H_3PO_4) and kept at 150-155 °C for 5 hours. The reaction was monitored by TLC. The spot for the starting compounds **5** was not completely disappeared. The reaction mixture was poured into ice water and neutralised with saturated $NaHCO_3$ solution to remove the excess of benzoic acid. The precipitate was filtered, dried and purified by column chromatography over silica gel using petroleum ether : ethyl acetate (94 6) mixture to get **8**. It was recrystallised using ethyl acetate.

2-(2-Chloro-9-methyl-12-phenyldibenzo[*b,g*][1,8]naphthyridin-11(6*H*)-ylidene)-1-phenyl ethanone (8a). Pale yellow prisms, Yield 25%, 0.1180 g, mp 190-192 ºC, IR (KBr) ν_{max} (cm^{-1}) 3245, 1596, 1517, 1112, ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 2.49 (3H, s, C9-CH_3), 7.43-8.47 (17H, m, C1, C3, C4, C7, C8, C10, C2', C3', C4', C5', C6', C2", C3", C4", C5"- C6"-H and olefinic proton), 8.98 (1H, b s, N6-H) ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 21.1, 118.7, 119.1, 122.0, 124.7, 124.9, 125.2, 125.5, 125.8, 126.0, 127.1, 127.4, 127.8, 128.2, 128.6, 128.9, 129.3, 129.5, 130.2, 130.6, 132.6, 135.9, 136.4, 142.8, 144.2, 150.7, 186.1, MS, (*m/z*) (%) 472 (M^+, 100), 474 (M+2, 34), 457 (80), 386 (35), 371 (60), 351 (30), 246 (25), 105 (48), 77 (48), Anal. Calcd for $C_{31}H_{21}ClN_2O$ C, 78.72, H, 4.47, N, 5.92. Found C, 79.00 H, 4.27 N, 5.88%.

2-(2-Chloro-7-methyl-12-phenyldibenzo[*b,g*][1,8]naphthyridin-11(6*H*)-ylidene)-1-phenyl ethanone (8b). Pale yellow prisms Yield 28%, 0.132 g, mp 187-189 ºC IR (KBr) ν_{max} (cm^{-1}) 3340, 1646, 1529, 1079, ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 2.57 (3H, s, C7-CH_3), 7.49-8.50 (17H, m, C1, C3, C4, C8, C9, C10, C2', C3', C4', C5', C6', C2", C3", C4", C5", C6"-H and olefinic proton), 8.92 (1H, b s, N6-H) ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 18.6, 117.7, 118.1, 122.9, 123.9, 124.1, 125.6, 126.5, 127.2, 128.6, 129.0, 129.2, 129.9, 130.2, 130.6, 131.4, 131.8, 132.0, 132.4, 133.1, 134.4, 142.3, 149.5, 151.9, 185.4, MS, (*m/z*) (%) 472 (M^+, 100), 474 (M+2, 34), 457 (80), 386 (35), 371 (60), 351 (30), 246 (25), 105 (48), 77 (48) Anal. Calcd for $C_{31}H_{21}ClN_2O$ C, 78.72; H, 4.47. N, 5.92. Found C, 79.02, H, 4.60, N, 6.00%.

2-(2,9-Dichloro-12-phenyldibenzo[*b,g*][1,8]naphthyridin-11(6*H*)-ylidene)-1-phenylethanone (8c). Pale yellow spongy mass, Yield 20%, 0.098 g, mp 193-195 ºC ; IR ν_{max} (cm^{-1}) 3241, 1617, 1517, 1084, ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 7.45-8.47 (17H, m, C1, C3, C4, C7, C8, C10, C2', C3', C4', C5', C6', C2", C3", C4", C5", C6"-H and olefinic proton), 9.03 (1H, bs, N6-H), ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 116.1, 118.6, 122.1, 122.8, 123.9, 124.4, 125.2, 125.4, 125.8, 126.2, 126.9, 127.1, 127.6, 128.2, 105 (48), 77 (48), Anal. Calcd for $C_{30}H_{18}Cl_2N_2O$ C, 73.03, H, 3.67, N, 5.67. Found C, 73.02, H, 3.73, N, 5.58%.

The above same procedure was demonstrated with 0.002 mol of benzoic acid. Now the starting material spot on TLC was complete disappeared. The same product was obtained, however the yield was appreciably increased.

2-(2-Chloro-9-methyl-12-phenyldibenzo[*b,g*][1,8]naphthyridin-11(6*H*)-ylidene)-1-phenyl ethanone (8a). Yield 40%, 0.189 g.

2-(2-Chloro-7-methyl-12-phenyldibenzo[*b,g*][1,8]naphthyridin-11(6*H*)-ylidene)-1-phenyl ethanone (8b). Yield 42%, 0.198 g.

2-(2,9-Dichloro-12-phenyldibenzo[*b,g*][1,8]naphthyridin-11(6*H*)-ylidene)-1-phenylethanone (8c). Yield 38%, 0.186 g.

General procedure for the preparation of 4-methyl-2-(4'-methyl-phenylamino)quinoline (10)

A mixture of appropriate 2-chloro-4-methylquinoline **1** (0.010 mol) and *p*-toluidine **9** (0.010 mol) was heated under neat condition at 160 ºC for half an hour. The product obtained was washed with water, dried purified by column chromatography over silica gel and eluted with ethyl acetate methanol mixture (95 5) to get **10**. It was recrystallised using methanol.

4,6-Dimethyl-2-(4'-methyl-phenylamino)quinoline (10a). Pale yellow prisms, Yield 70%, 1.834 g, mp 118-120 ºC, IR (KBr) ν_{max} (cm^{-1}) 3445, 1596, 1517, 1112, ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 2.35 (3H, s, C4'-CH_3), 2.57 (3H, s, C6-CH_3), 2.63 (3H, s, C4-CH_3), 6.62 (1H, b s, C2-NH), 6.74 (1H, s, C3-H), 7.17-7.68 (7H, m, C5, C7, C8, C2' C3' C5' and C6'-H) ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 19.8, 21.4, 21.9, 111.2, 120.7, 121.2, 121.8, 128.7, 129.6, 130.0, 132.3, 132.6, 136.5, 143.5, 147.3, 161.7, MS, (*m/z*) (%) 262 (M^+ 100) 261 (30), 246 (25), 245 (10), 232 (10), 122 (15), 77 (25), 65 (20), Anal. Calcd. for $C_{18}H_{18}N_2$ C, 82.40, H, 6.91, N, 10.67, Found C, 82.57, H, 6.71. N, 10.72%.

4,8-Dimethyl-2-(4'-methyl-phenylamino)quinoline (10b). Pale yellow prisms, Yield 75%, 1.965 g, mp 125-127 ºC, IR (KBr) ν_{max} (cm^{-1}) 3340, 1600, 1529, 1079, ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 2.35 (s, 3H, C4'-CH_3), 2.65 (s, 3H, C8-CH_3), 2.77 (s, 3H, C4-CH_3), 6.62 (b s, 1H, C2-NH), 6.77 (s, 1H, C3-H), 7.17-7.71 (m, 7H, C5, C6, C7, C2' C3' C5', C6'-H) ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 19.4, 21.8, 110.4, 120.6, 121.4, 122.2, 122.8, 123.2, 129.8, 131.0, 134.4, 137.5, 144.5, 154.4, 162.9, MS, (*m/z*) (%) 262 (M^+ 100) 261 (45), 246 (40), 245 (15), 232 (15), 123 (22), 77 (12), 65 (12); Anal. Calcd. for $C_{18}H_{18}N_2$ C, 82.40, H, 6.91, N, 10.67. Found C, 82.37, H, 6.92, N 10.71%.

6-Chloro-4-methyl-2-(4'-methyl-phenylamino)quinoline (10c). Pale yellow spongy mass, Yield 68%, 1.917 g, mp 130-132 ºC. IR (KBr) ν_{max} (cm^{-1}) 3241, 1617, 1517, 1084 ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 2.40 (s, 3H, C4'-CH_3), 2.77 (s, 3H, C4-CH_3), 6.62 (b s, 1H, C2-NH), 6.66 (s, 1H, C3-H), 7.19-7.72 (m, 7H, C5, C7, C8, C2' C3' C5' and C6'-H) ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 19.7, 21.6, 111.6, 118.3, 121.4, 122.6, 123.4, 126.4, 127.6, 129.7, 132.4, 135.1, 142.5, 146.7, 162.3, MS, (*m/z*) (%) 284/282 (34/100) 267 (22) 265 (10) 247 (15) 232 (18) 77 (50) 65 (33) 43 (56), Anal. Calcd. for $C_{17}H_{15}ClN_2$ C, 72.21, H, 5.34, N, 9.90, Found C, 72.45, H, 5.23, N, 9.85%.

General procedure for the preparation of 2-(2-methyl-12-phenyldibenzo[*b,g*][1,8]naphthyridin-11(6*H*)-ylidene)-1-phenylethanone (11)

An appropriate mixture of 4,4'-dimethyl-2-(*N*-phenylamino)quinoline **10** (0.0010 mol) and benzoic acid (0.0011 mol) was added to polyphosphoric acid (3 g of P_2O_5 in 1.5 mL of H_3PO_4) and kept at 160 °C for 5 hours. The reaction was monitored by TLC. The spot for the starting compounds **10** was not completely disappeared. The reaction mixture was poured into ice water and neutralised with saturated $NaHCO_3$ solution to remove the excess of benzoic acid. The precipitate was filtered, dried and purified by column chromatography over silica gel using petroleum ether ethyl acetate (99 1) mixture to get **11**. It was recrystallised using ethyl acetate.

2-(2,9-Dimethyl-12-phenyldibenzo[*b,g*][1,8]naphthyridin-11(6*H*)-ylidene)-1-phenylethanone (11a). Pale yellow prisms, Yield 22%, 0.099 g, mp 185-187 ºC, IR (KBr) ν_{max} (cm^{-1}) 3245, 1596, 1517, 111, ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 2.41 (s, 3H, C2-CH_3), 2.49 (s, 3H, C9-CH_3), 7.40-8.48 (m, 17H, C1, C3, C4, C7, C8, C10, C2', C3', C4', C5', C6', C2", C3", C4", C5", C6"-H and olefinic proton), 9.12 (b s, 1H, N6-H) ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 20.5, 22.3, 118.5, 119.7, 123.9, 124.7, 127.1, 127.5, 127.7, 128.5, 128.7, 128.9, 129.0, 129.2, 129.8, 129.9, 130.2, 130.8, 131.2, 132.2, 132.5, 133.8, 134.5, 136.7, 140.5, 149.9, 151.2, 188.5, MS, (*m/z*) (%) 452 (M^+, 100), 437 (80), 386 (35), 371 (60), 351 (30), 246 (25), 105 (48), 77 (48), Anal. Calcd for $C_{32}H_{24}N_2O$ C, 84.93, H, 5.34. N, 6.18. Found C, 84.60. H, 5.39, N, 6.31%.

2-(2,7-Dimethyl-12-phenyldibenzo[*b,g*][1,8]naphthyridin-11(6*H*)-ylidene)-1-phenylethanone (11b). Pale yellow prisms, Yield 25%, 0.113 g, mp 187-189 ºC, IR (KBr) ν_{max} (cm^{-1}) 3340, 1600, 1529, 107, ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 2.41 (3H, s, C2-CH_3), 2.77 (3H, s, C7-CH_3), 7.46-8.51 (17H, m, C1, C3, C4, C8, C9, C10, C2', C3', C4', C5', C6', C2", C3", C4", C5", C6"-H and olefinic proton), 9.07 (1H, b s, N6-H) ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 18.2, 21.8, 118.2, 119.6, 124.6, 124.9, 125.3, 126.8, 127.4, 127.8, 128.4, 128.8, 129.0, 129.2, 129.9, 130.2, 130.4, 130.6, 131.4, 131.8, 133.0, 133.7, 134.8, 135.0, 140.2, 149.9, 151.5, 189.9. MS, (*m/z*) (%) 452 (M^+, 100), 437 (80), 386 (35), 371 (60), 351 (30), 246 (25), 105 (48), 77 (48), Anal. Calcd for $C_{32}H_{24}N_2O$ C, 84.93, H, 5.34, N, 6.18. Found C, 84.68, H, 5.21, N, 6.09%.

2-(9-Chloro-2-methyl-12-phenyldibenzo[*b,g*][1,8]naphthyridin-11(6*H*)-ylidene)-1-phenyl ethanone (11c). Pale yellow spongy mass, Yield 18%, 0.085 g, mp 193-195 ºC, IR (KBr) ν_{max} (cm^{-1}) 3241, 1617, 1517, 1084; ^{1}H-NMR (400 MHz, $CDCl_3$) δ_H 2.41 (3H, s, C2-CH_3), 7.43-8.48 (17H, m, C1, C3, C4, C7, C8, C10, C2', C3', C4', C5', C6', C2", C3", C4", C5", C6"-H and olefinic proton), 9.13 (1H, b s, N6-H) ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 20.2, 118.5, 119.9, 123.7, 124.5, 126.7, 127.1, 127.5, 127.7, 127.9, 128.0, 128.7, 129.5, 129.7, 129.9, 130.1, 131.0, 131.6, 131.9, 132.2, 133.3, 134.5, 140.7, 149.9, 151.2, 187.6, MS,(*m/z*) (%) 472 (M^+, 100), 474 (M+2, 34), 457 (80), 386 (35), 371 (60), 351 (30), 246 (25), 105 (48), 77 (48) Anal. Calcd for $C_{31}H_{21}ClN_2O$ C, 78.72, H, 4.47; N, 5.92. Found C, 79.02, H, 4.60, N, 6.00%.

The above same procedure was demonstrated with 0.002 mol of benzoic acid. Now the starting material spot on TLC was complete disappeared. The same product was obtained, however the yield was appreciably increased.

2-(2,9-Dimethyl-12-phenyldibenzo[*b,g*][1,8]naphthyridin-11(6*H*)-ylidene)-1-phenylethanone (11a). Yield 41%, 0.185 g.
2-(2,7-Dimethyl-12-phenyldibenzo[*b,g*][1,8]naphthyridin-11(6*H*)-ylidene)-1-phenylethanone (11b). Yield 42%, 0.190 g.
2-(9-Chloro-2-methyl-12-phenyldibenzo[*b,g*][1,8]naphthyridin-11(6*H*)-ylidene)-1-phenyl ethanone (11c). Yield 37%, 0.175 g.

General procedure for the preparation of 2[(2'-acetylphenyl)amino]-4-methylquinoline (12)
An appropriate 2-chloro-4-methylquinoline **1** (0.004 mol) was reacted with *o*-aminoacetophenone **2** (0.004 mol) under neat condition at 160 °C for half an hour. The product was washed with water, adsorbed and purified using silica gel column chromatography and eluted with petroleum ether ethyl acetate (98 2) mixture to get **13** which was then recrystallised using methanol.
2[(2'-Acetylphenyl)amino]-4,6-dimethylquinoline (12a). Pale yellow prisms, Yield 0.788 g, 68%, mp 118-120 ºC, IR (KBr) ν_{max} (cm^{-1}) 3245, 1596, 1517, 1112 ^{1}H-NMR (400 MHz, $CDCl_3$) δ_H 2.60 (3H, s, $COCH_3$), 2.66 (3H, s, C6-CH_3), 2.76 (3H, s, C4-CH_3), 6.67 (1H, s, C3-H), 7.05 7.94 (6H, m, C5, C7, C8, C3', C4', C5'-H), 9.50 (1H, d, C6'-H, *J* = 8.99 Hz), 11.80 (1H, b s, NH); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 19.4, 22.1, 28.9, 111.8, 118.1, 118.3, 119.2, 120.5, 120.8, 127.8, 128.9, 129.5, 131.7, 133.2, 143.9, 147.2, 152.8, 154.9, 196.6. MS, (*m/z*) (%) 290 (M^+, 100), 289 (10), 276 (20), 247 (15), 156 (8), 143 (18), 76 (16), Anal. Calcd for $C_{19}H_{18}N_2O$ C, 78.59, H, 6.24, N, 9.64. Found C, 78.55, H, 6.32, N, 9.56%.
2[(2'-Acetylphenyl)amino]-4,8-dimethylquinoline (12b). Pale yellow prisms, Yield 70%, 0.812 g, mp 125-127 ºC, IR (KBr) ν_{max} (cm 3390, 1635, 1529, 1079 ^{1}H-NMR (400 MHz, $CDCl_3$) δ_H 2.62 (3H, s, $COCH_3$), 2.70 (3H, s, C8-CH_3), 2.76 (3H, s, C4-CH_3), 6.83 (1H, s, C3-H), 6.94 7.93 (6H, m, C5, C6, C7, C3', C4', C5'-H), 9.57 (1H, d, C6'-H, *J* = 8.87 Hz), 11.80 (1H, b s, NH), ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 17.8, 19.2, 28.3, 110.7, 117.5, 118.2, 118.9, 120.2, 121.6, 122.8, 128.4, 128.9, 132.1, 132.6, 144.8, 145.7, 154.1, 163.5, 199.1, MS, (*m/z*) (%) 290 (M^+, 100), 289 (8), 276 (24), 247 (18), 156 (12), 143 (6), 76 (8), Anal. Calcd for $C_{19}H_{18}N_2O$ C, 78.59, H, 6.24, N 9.64. Found C, 78.77, H, 6.19, N, 9.73%.

X-Ray Crystallographic data
Crystallographic data of the structure **12b** in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication. CCDC No. 755306. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK. Or email: deposit@ccdc.cam.ac.UK.

Acknowldegements

The authors thank IISc, Bangalore, MKU, Madurai for NMR spectra, IICT, Hyderabad for mass spectral data and IIT Madras, Chennai for single crystal XRD data.

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