Synthesis of Novel Substituted Dibenzonaphthyridines

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4-Chloro-2-methylquinolines **1a** – **d** on reaction with *p*-toluidine afforded 2,4′-dimethyl-4-(*N*-phenylamino)quinolines **2a** – **d** which on reaction with aliphatic and aromatic carboxylic acids yielded the respective 7-substituted dibenzonaphthyridines **3a** – **d** and **4a** – **d** whereas a heterocyclic acid afforded **5a** – **c** and **6a** – **c**.

Key words: 4-Chloro-2-methylquinolines, 2,4′-Dimethyl-4-(*N*-phenylamino)quinolines, Acetic Acid, Benzoic Acid, 2-Chloro-8-methylquinoline-3-carboxylic Acid

Introduction

Heterocyclic compounds are very widely distributed in nature and are essential to life as they play a vital role in the metabolism of living cells. There are a vast number of pharmacologically active heterocyclic compounds of which many are in regular therapeutic usage. Among various heterocyclic compounds, quinoline-based drugs such as quinine, chloroquine, pamaquine and quinacrine are well known for their antimalarial property. In this regard some of the anilinoquinolines particularly attracted considerable attention [1]. The interest in naphthyridine derivatives is due to the exceptionally broad spectrum of their biological activities. They are used for the diagnosis and therapy of diseases of humans including AIDS [2, 3] and cancer [4]. Some of the dibenzonaphthyridines, *i. e.* quinoline dimers, have been shown to possess various biological activities like antimicrobial [5] and anticancer [6] activity, and are potent and selective 3-phosphoinostide-dependent kinase-I inhibitors [7]. A detailed survey of the literature points out that many reactions of chloroquinolines aimed to get substitution products possessing biological activity [8, 9]. Since the discovery of the first naphthyridine by Reissert in the year 1893 [10], many procedures have been evolved for the synthesis of simple benzo- and dibenzonaphthyridines [11 – 14], but only very few accomplished the construction through anilinoquinolines, *i. e.* (*N*-phenylamino)quinolines [15, 16].

Herein we opt to synthesize the various 3-substituted dibenzonaphthyridines holding a diversity of substituents such as aliphatic, aromatic and heterocyclic moieties utilizing anilinoquinolines, namely 2,4′-dimethyl-4-(*N*-phenylamino)quinolines **2a** – **d**, as precursors.

Results and Discussion

With the objective to derive 2,4′-dimethyl-4-(*N*-phenylamino)quinolines **2a** – **d** which could be used as potential precursors to achieve the target molecules, 4-chloro-2-methyl-quinolines **1a** – **d** were reacted with *p*-toluidine under neat condition at 160 °C. Compounds **2a** – **d** were found to be in equilibrium with their imino forms (ratio of amino form : imino form is 1 : 1) from ^{1}H NMR spectroscopy (Scheme 1).

After obtaining the potential intermediates **2** we focused our attention to react them with aliphatic, aromatic and heterocyclic acids thereby anticipating to get these moieties as substitutents of the respective dibenzonaphthyridines. Hence **2a** – **d** were reacted with acetic acid and benzoic acid in the presence of PPA as catalyst at 160 °C each for 5 h to afford the respective products, 6,7,9-trimethyldibenzo[*b,h*][1,6]naphthyridines **3a** – **d** and 6,9-dimethyl-7-phenyldibenzo[*b,h*][1,6]naphthyridines **4a** – **d**.

Since, both the quinoline and naphthyridine chemistry are well known for their biological importance, we wanted to combine the quinoline moiety with the naphthyridine unit. Therefore quinolines **2** were reacted with 2-chloro-8-methylquinoline-3-carboxylic acid [17] for 8 h to afford two products. The less polar products (35 %) eluted with a petroleum ether : ethyl acetate (99 : 1) mixture answered Lassaigne's test for chlorine, and finally their structure was

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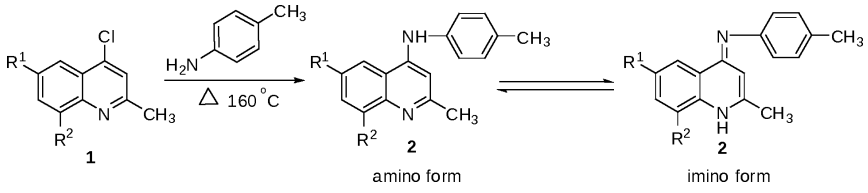
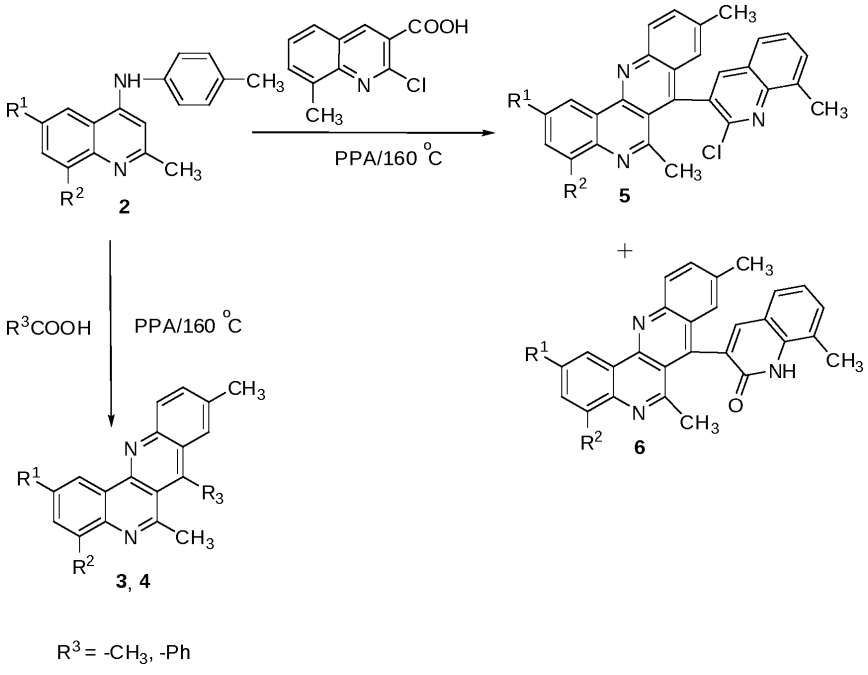


1, **2a**: $R^1 = CH_3$, $R^2 = H$
b: $R^1 = H$, $R^2 = CH_3$
c: $R^1 = Cl$, $R^2 = H$
d: $R^1 = H$, $R^2 = H$

Scheme 1.



2, **3**, **4a**: $R^1 = CH_3$, $R^2 = H$
b: $R^1 = H$, $R^2 = CH_3$
c: $R^1 = Cl$, $R^2 = H$
d: $R^1 = H$, $R^2 = H$

5, **6a**: $R^1 = CH_3$, $R^2 = H$
b: $R^1 = H$, $R^2 = CH_3$
c: $R^1 = Cl$, $R^2 = H$

Scheme 2.

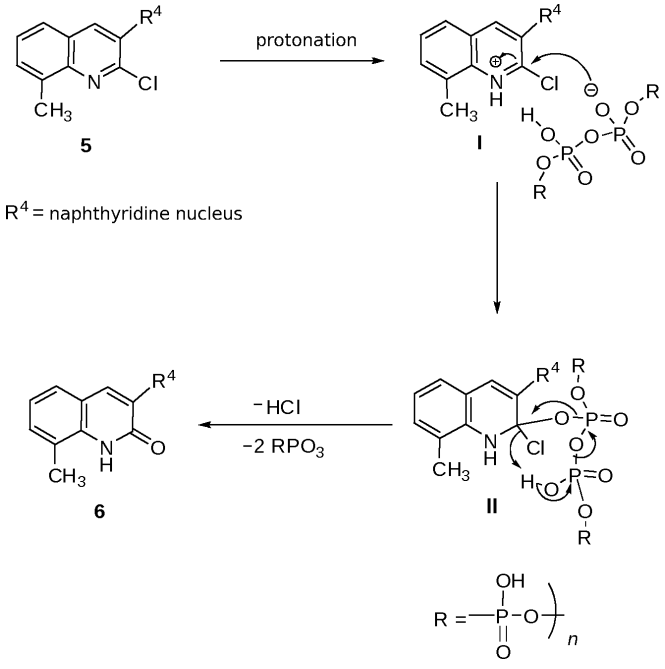
assigned as 6,9-dimethyl-7-(2-chloro-8-methylquinolin-3-yl)dibenzo[*b,h*][1,6]naphthyridines **5a – c**. The more polar products (15 %) eluted with a petroleum ether : ethyl acetate (95 : 5) mixture showed a broad singlet around δ = 9.3 ppm in their ^{1}H NMR spectra. The appearance of a carbonyl stretching vibration around 1640 cm^{-1} in the IR spectra and the presence of a carbonyl carbon signal around δ = 170 ppm in the ^{13}C NMR spectra revealed that the products formed were 6,9-dimethyl-7-(8-methylquinolin-2[1*H*]-on-3-yl)dibenzo[*b,h*][1,6]naphthyridines **6a – c** (Scheme 2).

We assumed that the minor compounds **6** were definitely formed from the major compounds **5**. The mechanism for the conversion of **5** to **6** under PPA condition (Scheme 3) might involve the protonation of the ring nitrogen of **5** to give the intermediate **I** followed by the *ipso* attack of the $^-OP_2O_6HR_2$ ion at the C-2′ carbon of the quinoline nucleus to yield the intermediate **II**. Subsequent elimination of HCl would afford **6**.

The conversion of **5** to **6** was also done with 6 N HCl to get the same result. The reverse conversion of **6** to **5** through the familiar chlorination reaction using $POCl_3$ was also confirmed in the present case (Scheme 4).

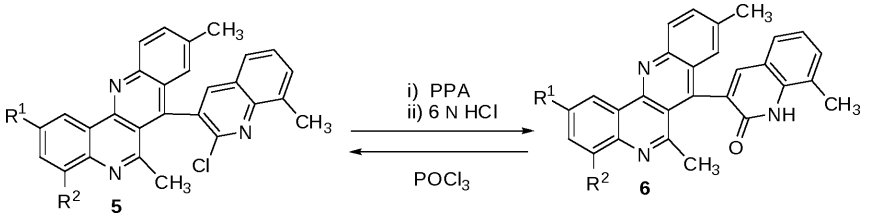
Experimental Section

Melting points (m. p.) were determined on a Mettler FP 51 apparatus (Mettler Instruments, Switzerland) and are uncorrected. IR spectra were recorded on a Schimadzu FTIR-8201PC spectrophotometer (Schimadzu, Japan) using a KBr disc. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker AMX 400 [400 MHz (^{1}H) and 100 MHz (^{13}C)] spectrometer using tetramethylsilane (TMS) as an internal reference. The chemical shifts are expressed in parts per million (ppm). Mass spectra (MS) were recorded on an AutoSpec EI+ Shimadzu QP 2010 PLUS GC-MS mass spectrometer. Microanalyses were performed with a Vario EL III model CHNS analyzer (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



5, **I**, **II**, **6a**: $R^1 = CH_3$, $R^2 = H$
b: $R^1 = H$, $R^2 = CH_3$
c: $R^1 = Cl$, $R^2 = H$
d: $R^1 = H$, $R^2 = H$

Scheme 3.



5, **6a**: $R^1 = CH_3$, $R^2 = H$
b: $R^1 = H$, $R^2 = CH_3$
c: $R^1 = Cl$, $R^2 = H$
d: $R^1 = H$, $R^2 = H$

Scheme 4.

with petroleum ether, ethyl acetate and methanol as developing solvents.

*Preparation of 2,4′-dimethyl-4-(N-phenylamino)quinolines **2**, general procedure*

4-Chloro-2-methylquinoline (**1**, 0.002 mol) was reacted with *p*-toluidine (0.002 mol) under neat condition at 160 °C for half an hour. The product obtained was washed with water, dried, and purified by column chromatography over silica gel using an ethyl acetate : methanol (95 : 5) mixture to get **2** as a white solid. It was recrystallized using methanol.

*2,6,4′-Trimethyl-4-(N-phenylamino)quinoline (**2a**)*

M. p. > 300 °C. – Yield: 0.262 g (50 %). – IR (KBr): ν = 3405 (NH), 1601, 1541 cm^{-1}. – ^1H NMR (400 MHz, [D_6]DMSO): δ = 2.41 (s, 3 H, 4′-CH_3), 2.51 (s, 3 H, 6-CH_3), 2.62 (s, 3 H, 2-CH_3), 6.49 (s, 1 H, 3-H), 7.25 – 7.36 (m, 4 H, 2′-H, 3′-H, 5′-H, 6′-H), 7.43 (d, J = 8.20 Hz, 1 H, 7-H), 8.03 (d, J = 8.80 Hz, 1 H, 8-H), 8.49 (s, 1 H, 5-H), 11.20 (s, 1 H, C_4-NH, amino form), 13.08 (s, 1H, N-1-H, imino form; the ratio of amino form : imino form is 1 : 1). – ^{13}C NMR (100 MHz, [D_6]DMSO): δ = 17.12 (4′-CH_3), 18.25 (6-CH_3), 19.80 (2-CH_3), 109.03 (C-3), 114.36 (C2′, C6′), 121.32 (C3′, C5′), 122.18 (C-5), 125.55 (C4′), 126.89 (C-8), 127.42 (C-7), 132.21 (C-6), 132.49 (C-4a), 143.67 (C1′), 148.93 (C-4), 149.56 (C-8a), 153.34 (C-2). – MS (EI, 70 eV): *m/z* (%) = 262 (100) $[M]^+$. – $C_{18}H_{18}N_2$ (262.35): calcd. C 82.44, H 6.87, N 10.69; found C 82.37, H 6.91, N 10.72.

*2,8,4′-Trimethyl-4-(N-phenylamino)quinoline (**2b**)*

M. p. > 300 °C. – Yield: 0.236 g (45 %). – IR (KBr): ν = 3397 (NH), 1599, 1545 cm^{-1}. – ^1H NMR (400 MHz, [D_6]DMSO): δ = 2.38 (s, 3 H, 4′-CH_3), 2.67 (s, 3 H, 8-CH_3), 2.70 (s, 3 H, 2-CH_3), 6.63 (s, 1 H, 3-H), 7.30 – 7.37 (m, 4 H, 2′-H, 3′-H, 5′-H, 6′-H), 7.64 (m, 1 H, 6-H), 7.82 (d, J = 7.08 Hz, 1 H, 7-H), 8.62 (d, J = 7.89 Hz, 1 H, 5-H), 10.81 (s, 1 H, C_4-NH, amino form), 12.51 (s, 1 H, N-1-H, imino form; the ratio of amino form : imino form is 1 : 1). –

^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 17.12 (4′-CH$_3$), 18.97 (8-CH$_3$), 20.13 (2-CH$_3$), 108.69 (C-3), 114.93 (C2′, C6′), 121.31 (C3′, C5′), 123.05 (C-5), 125.55 (C4′), 127.16 (C-6), 127.85 (C-7), 132.99 (C-8), 133.64 (C-4a), 144.08 (C1′), 149.44 (C-4), 150.31 (C-8a), 152.96 (C-2). – MS (EI, 70 eV): *m/z* (%) = 262 (100) [M]$^+$. – $C_{18}H_{18}N_2$ (262.35): calcd. C 82.44, H 6.87, N 10.69; found C 82.56, H 6.99, N 10.45.

*6-Chloro-2,4′-dimethyl-4-(N-phenylamino)quinoline (**2c**)*

M. p. > 300 °C. – Yield: 0.226 g (40 %). – IR (KBr): ν = 3409 (NH), 1597, 1543 cm^{-1}. – ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 2.36 (s, 3 H, 4′-CH$_3$), 2.65 (s, 3 H, 2-CH$_3$), 6.55 (s, 1 H, 3-H), 7.24 – 7.34 (m, 4 H, 2′-H, 3′-H, 5′-H, 6′-H), 7.64 (d, *J* = 8.40 Hz, 1 H, 7-H), 8.02 (d, *J* = 8.68 Hz, 1 H, 8-H), 8.69 (s, 1 H, 5-H), 10.94 (s, 1 H, C$_4$-NH, amino form), 13.23 (s, 1 H, N-1-H, imino form; the ratio of amino form : imino form is 1 : 1). – ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 17.12 (4′-CH$_3$), 20.14 (2-CH$_3$), 109.27 (C-3), 114.41 (C2′, C6′), 121.38 (C3′, C5′), 122.62 (C-5), 125.55 (C4′), 127.92 (C-8), 128.54 (C-7), 130.98 (C-6), 132.81 (C-4a), 143.70 (C1′), 148.64 (C-4), 149.05 (C-8a), 153.16 (C-2). – MS (EI, 70 eV): *m/z* (%) = 284/282 (34/100) [M+2]/[M]$^+$. – $C_{17}H_{15}N_2Cl$ (282.77): calcd. C 72.34, H 5.32, N 9.93; found C 72.45, H 5.23, N 9.85.

*2,4′-Dimethyl-4-(N-phenylamino)quinoline (**2d**)*

M. p. > 300 °C. – Yield: 0.213 g (43 %). – IR (KBr): ν = 3406 (NH), 1590, 1536 cm^{-1}. – ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 2.35 (s, 3 H, 4′-CH$_3$), 2.68 (s, 3 H, 2-CH$_3$), 6.41 (s, 1 H, 3-H), 7.27 – 7.38 (m, 4 H, 2′-H, 3′-H, 5′-H, 6′-H), 7.52 – 7.84 (m, 2 H, 6-H, 7-H), 8.06 (d, *J* = 8.26 Hz, 1 H, 8-H), 8.56 (d, *J* =7.95 Hz, 1 H, 5-H), 10.97 (s, 1H, C$_4$-NH, amino form), 12.81 (s, 1H, N-1-H, imino form; the ratio of amino form : imino form is 1 : 1). – ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 17.12 (4′-CH$_3$), 19.93 (2-CH$_3$), 108.85 (C-3), 114.24 (C2′, C6′), 121.32 (C3′, C5′), 123.10 (C-5), 125.86 (C4′), 126.86 (C-6), 127.25 (C-7), 128.43 (C-8), 134.07 (C-4a), 144.82 (C1′), 148.83 (C-4), 150.12 (C-8a), 153.20 (C-2). – MS (EI, 70 eV): *m/z* (%) = 248 (100) [M]$^+$. – $C_{17}H_{16}N_2$ (248.32): calcd. C 82.26, H 6.45, N 11.29; found C 82.35, H 6.38, N 11.27.

*Reaction of **2** with acetic acid*

*Preparation of 6,7,9-trimethyldibenzo[b,h][1,6]naphthyridine (**3**), general procedure*

A mixture of 2,4′-dimethyl-4-(*N*-phenylamino)quinoline (**2**, 0.001 mol) and acetic acid (0.0011 mol) was added to polyphosphoric acid (1 g of P_2O_5 and 0.5 mL H_3PO_4) and heated at 160 °C for 5 h. The reaction mixture was poured into excess ice water, extracted with ethyl acetate and purified using silica gel column chromatography, and the product eluted with a petroleum ether : ethyl acetate (98 : 2) mixture to get **3**, which was recrystallized using ethanol.

*2,6,7,9-Tetramethyldibenzo[b,h][1,6]naphthyridine (**3a**)*

M. p. 222 – 224 °C. – Yield: 0.092 g (32 %). – IR (KBr): ν = 1624 and 1594 (C=N), 1535, 1450 cm^{-1}. – ^{1}H NMR (400 MHz, CDCl$_3$): δ = 2.54 (s, 3 H, 9-CH$_3$), 2.77 (s, 3 H, 2-CH$_3$), 3.11 (s, 3 H, 7-CH$_3$), 3.19 (s, 3 H, 6-CH$_3$) 7.55 – 8.10 (m, 4 H, 3-H, 4-H, 8-H, 10-H), 8.18 (d, *J* = 8.53 Hz, 1 H, 11-H), 9.13 (s, 1 H, 1-H). – ^{13}C NMR (100 MHz, CDCl$_3$): δ = 17.47 (9-CH$_3$), 21.85 (2-CH$_3$), 25.43 (7-CH$_3$), 29.67 (6-CH$_3$), 117.14 (C-7a), 122.04 (C-6a), 122.82 (C-8), 125.85 (C-1), 126.79 (C-7), 128.26 (C-9), 128.42 (C-3), 128.92 (C-4), 130.95 (C-10), 131.51 (C-11), 132.33 (C-2), 134.51 (C-12b), 136.67 (C-11a), 146.72 (C-4a), 147.32 (C-12a), 158.66 (C-6). – MS (EI, 70 eV): *m/z* (%) = 286 (100) [M]$^+$. – $C_{20}H_{18}N_2$ (286.37): calcd. C 83.92, H 6.29, N 9.79; found C 83.82, H 6.09, N 10.09.

*4,6,7,9-Tetramethyldibenzo[b,h][1,6]naphthyridine (**3b**)*

M. p. 220 – 222 °C. – Yield: 0.086 g (30 %). – IR (KBr): ν = 1628 and 1599 (C=N), 1531, 1460 cm^{-1}. – ^{1}H NMR (400 MHz, CDCl$_3$): δ = 2.58 (s, 3 H, 9-CH$_3$), 2.81 (s, 3 H, 4-CH$_3$), 3.16 (s, 3 H, 7-CH$_3$), 3.24 (s, 3 H, 6-CH$_3$) 7.53 – 8.07 (m, 4 H, 2-H, 3-H, 8-H, 10-H)), 8.21 (d, *J* = 8.60 Hz, 1 H, 11-H), 9.11 (d, *J* = 7.64 Hz, 1 H, 1-H). – ^{13}C NMR (100 MHz, CDCl$_3$): δ = 17.47 (9-CH$_3$), 22.68 (4-CH$_3$), 25.45 (7-CH$_3$), 29.75 (6-CH$_3$), 117.14 (C-7a), 122.04 (C-6a), 122.82 (C-8), 126.16 (C-1), 126.79 (C-7), 128.26 (C-9), 127.33 (C-2), 128.64 (C-3), 130.95 (C-10), 131.51 (C-11), 132.83 (C-4), 134.82 (C-12b), 136.67 (C-11a), 147.09 (C-4a), 147.50 (C-12a), 158.87 (C-6). – MS (EI, 70 eV): *m/z* (%) = 286 (100) [M]$^+$. – $C_{20}H_{18}N_2$ (286.37): calcd. C 83.92, H 6.29, N 9.79; found C 83.86, H 6.12, N 10.02.

*2-Chloro-6,7,9-trimethyldibenzo[b,h][1,6]naphthyridine (**3c**)*

M. p. 228 – 230 °C. – Yield: 0.089 g (29 %). – IR (KBr): ν = 1630 and 1601 (C=N), 1537, 1455 cm^{-1}. – ^{1}H NMR (400 MHz, CDCl$_3$): δ = 2.55 (s, 3 H, 9-CH$_3$), 3.15 (s, 3 H, 7-CH$_3$), 3.20 (s, 3 H, 6-CH$_3$) 7.50 – 8.15 (m, 4 H, 3-H, 4-H, 8-H, 10-H), 8.16 (d, *J* = 8.48 Hz, 1 H, 11-H), 9.16 (s, 1 H, 1-H). – ^{13}C NMR (100 MHz, CDCl$_3$): δ = 17.47 (9-CH$_3$), 25.42 (7-CH$_3$), 29.65 (6-CH$_3$), 117.14 (C-7a), 122.04 (C-6a), 122.82 (C-8), 125.62 (C-1), 126.79 (C-7), 128.26 (C-9), 128.05 (C-3), 128.78 (C-4), 130.95 (C-10), 131.51 (C-11), 132.83 (C-2), 134.26 (C-12b), 136.67 (C-11a), 146.01 (C-4a), 146.98 (C-12a), 158.18 (C-6). – MS (EI, 70 eV): *m/z* (%) = 308/306 (30/95) [M+2]/[M]$^+$. – $C_{19}H_{15}N_2Cl$ (306.79): calcd. C 74.51, H 4.90, N 9.15; found C 74.35, H 4.79, N 9.20.

*6,7,9-Trimethyldibenzo[b,h][1,6]naphthyridine (**3d**)*

M. p. 217 – 219 °C. – Yield: 0.082 g (30 %). – IR (KBr): ν = 1623 and 1596 (C=N), 1524, 1452 cm^{-1}. – ^1H NMR (400 MHz, $CDCl_3$): δ = 2.52 (s, 3 H, 9-CH_3), 3.12 (s, 3 H, 7-CH_3), 3.19 (s, 3 H, 6-CH_3) 7.48 – 8.09 (m, 5 H, 2-H, 3-H, 4-H, 8-H, 10-H), 8.15 (d, J = 8.42 Hz, 1 H, 11-H), 9.09 (d, J = 7.86 Hz, 1 H, 1-H). – ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.47 (9-CH_3), 25.40 (7-CH_3), 29.62 (6-CH_3), 117.14 (C-7a), 122.04 (C-6a), 122.82 (C-8), 125.04 (C-1), 126.75 (C-7), 126.94 (C-2), 127.26 (C-3), 128.06 (C-4), 128.26 (C-9), 130.95 (C-10), 131.51 (C-11), 134.13 (C-12b), 136.67 (C-11a), 146.34 (C-4a), 147.32 (C-12a), 158.54 (C-6). – MS (EI, 70 eV): *m/z* (%) = 272 (93) $[M]^+$. – $C_{19}H_{16}N_2$ (272.34): calcd. C 83.82, H 5.88, N 10.30; found C 83.74, H 5.77, N 10.49.

*Reaction of **2** with benzoic acid*

*Preparation of 6,9-dimethyl-7-phenyldibenzo[b,h][1,6] naphthyridines **4**, general procedure*

A mixture of 2,4′-dimethyl-4-(*N*-phenylamino)quinoline (**2**, 0.001 mol) and benzoic acid (0.0011 mol) was added to polyphosphoric acid (1 g of P_2O_5 and 0.5 mL H_3PO_4) and heated at 160 °C for 5 h. The reaction mixture was poured into ice water, neutralized with saturated sodium bicarbonate solution to remove the excess of benzoic acid, extracted with ethyl acetate and purified using silica gel column chromatography. The product was eluted with a petroleum ether : ethyl acetate (99 : 1) mixture to get **4**, which was recrystallized using ethanol.

*2,6,9-Trimethyl-7-phenyldibenzo[b,h][1,6]naphthyridine (**4a**)*

M. p. 222 – 224 °C. – Yield: 0.122 g (35 %). – IR (KBr): ν = 1630 and 1591 (C=N), 1552, 1448 cm^{-1}. – ^1H NMR (400 MHz, $CDCl_3$): δ = 2.46 (s, 3 H, 9-CH_3), 2.69 (s, 3 H, 2-CH_3), 3.16 (s, 3 H, 6-CH_3) 7.25 – 8.27 (m, 9 H, 3-H, 4-H, 8-H, 10-H, 2′-H, 3′-H, 4′-H, 5′-H, 6′-H), 8.18 (d, J = 8.53 Hz, 1 H, 11-H), 9.18 (s, 1 H, 1-H). – ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.75 (9-CH_3), 22.08 (2-CH_3), 29.78 (6-CH_3), 117.81 (C-7a), 121.23 (C-6a), 122.45 (C-8), 124.92 (C-2′, C-6′), 125.98 (C-3′, C-4′, C-5′), 126.46 (C-1), 127.12 (C-7), 128.41 (C-9), 128.56 (C-3), 129.45 (C-4), 130.08 (C-1′), 131.34 (C-10), 133.74 (C-11), 134.26 (C-2), 136.12 (C-12b), 139.24 (C-11a), 147.65 (C-4a), 148.31 (C-12a), 158.75 (C-6). – MS (EI, 70 eV): *m/z* (%) = 348 (100) $[M]^+$. – $C_{25}H_{20}N_2$ (348.44): calcd. C 86.21, H 5.75, N 8.40; found C 86.03, H 6.01, N 7.96.

*4,6,9-Trimethyl-7-phenyldibenzo[b,h][1,6]naphthyridine (**4b**)*

M. p. 220 – 222 °C. – Yield: 0.132 g (38 %). – IR (KBr): ν = 1627 and 1597 (C=N), 1530, 1457 cm^{-1}. – ^1H NMR (400 MHz, $CDCl_3$): δ = 2.49 (s, 3 H, 9-CH_3), 2.73 (s, 3 H, 4-CH_3), 3.18 (s, 3 H, 6-CH_3) 7.24 – 8.29 (m, 9 H, 2-H, 3-H, 8-H, 10-H, 2′-H, 3′-H, 4′-H, 5′-H, 6′-H), 8.21 (d, J = 8.51 Hz, 1 H, 11-H), 9.20 (d, 1 H, J = 7.44 Hz,1-H). – ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.75 (9-CH_3), 23.01 (4-CH_3), 30.04 (6-CH_3), 117.81 (C-7a), 121.23 (C-6a), 122.45 (C-8), 124.92 (C-2′, C-6′), 125.98 (C-3′, C-4′, C-5′), 126.13 (C-1), 127.12 (C-7), 128.41 (C-9), 128.16 (C-2), 128.83 (C-3), 130.08 (C-1′), 131.34 (C-10), 133.74 (C-11), 134.80 (C-4), 136.14 (C-12b), 139.24 (C-11a), 147.92 (C-4a), 148.39 (C-12a), 158.77 (C-6). – MS (EI, 70 eV): *m/z* (%) = 348 (100) $[M]^+$. – $C_{25}H_{20}N_2$ (348.44): calcd. C 86.21, H 5.75, N 8.40; found C 86.35, H 5.61, N 8.04.

*2-Chloro-6,9-dimethyl-7-phenyldibenzo[b,h][1,6]naphthyridine (**4c**)*

M. p. 228 – 230 °C. – Yield: 0.118 g (32 %). – IR (KBr): ν = 1632 and 1598 (C=N), 1537, 1454 cm^{-1}. – ^1H NMR (400 MHz, $CDCl_3$): δ = 2.45 (s, 3 H, 9-CH_3), 3.17 (s, 3 H, 6-CH_3), 7.22 – 8.22 (m, 9 H, 3-H, 4-H, 8-H, 10-H, 2′-H, 3′-H, 4′-H, 5′-H, 6′-H), 8.19 (d, J = 8.38 Hz, 1 H, 11-H), 9.25 (s, 1 H, 1-H). – ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.75 (9-CH_3), 29.85 (6-CH_3), 117.81 (C-7a), 121.23 (C-6a), 122.45 (C-8), 124.92 (C-2′, C-6′), 125.98 (C-3′, C-4′, C-5′), 126.31 (C-1), 127.12 (C-7), 128.41 (C-9), 128.22 (C-3), 129.27 (C-4), 130.08 (C-1′), 131.34 (C-10), 133.74 (C-11), 133.96 (C-2), 136.10 (C-12b), 139.24 (C-11a), 147.72 (C-4a), 148.56 (C-12a), 158.98 (C-6). – MS (EI, 70 eV): *m/z* (%) = 370/368 (35/100) [M+2]/$[M]^+$. – $C_{24}H_{17}N_2Cl$ (368.87): calcd. C 78.26, H 4.62, N 7.61; found C 78.35, H 4.73, N 7.50.

*6,9-Dimethyl-7-phenyldibenzo[b,h][1,6]naphthyridine (**4d**)*

M. p. 217 – 219 °C. – Yield: 0.117 g (35 %). – IR (KBr): ν = 1626 and 1600 (C=N), 1528, 1453 cm^{-1}. – ^1H NMR (400 MHz, $CDCl_3$): δ = 2.48 (s, 3 H, 9-CH_3), 3.14 (s, 3 H, 6-CH_3) 7.28 – 8.19 (m, 10 H, 2-H, 3-H, 4-H, 8-H, 10-H, 2′-H, 3′-H, 4′-H, 5′-H, 6′-H), 8.20 (d, J = 8.34 Hz, 1 H, 11-H), 9.19 (d, J = 7.86 Hz, 1 H, 1-H). – ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.75 (9-CH_3), 29.84 (6-CH_3), 117.81 (C-7a), 121.23 (C-6a), 122.45 (C-8), 124.92 (C-2′, C-6′), 125.98 (C-3′, C-4′, C-5′), 126.07 (C-1), 127.12 (C-7), 128.41 (C-9), 128.37 (C-2), 129.04 (C-3), 129.95 (C-4), 130.08 (C-1′), 131.34 (C-10), 133.74 (C-11), 136.10 (C-12b), 139.24 (C-11a), 147.72 (C-4a), 148.56 (C-12a), 158.98 (C-6). – MS (EI, 70 eV): *m/z* (%) = 334 (100) $[M]^+$. – $C_{24}H_{18}N_2$ (334.41): calcd. C 86.23, H 5.39, N 8.38; found C 86.09, H 5.50, N 8.41.

*Reaction of **2** with 2-chloro-8-methylquinoline-3-carboxylic acid*

*Preparation of 6,9-dimethyl-7-(2-chloro-8-methylquinolin-3-yl)dibenzo[b,h][1,6]naphthyridines **5** and 6,9-dimeth-*

*yl-7-(8-methylquinolin-2[1H]-on-3-yl)dibenzo[b,h][1,6] naphthyridines **6**, general procedure*

A mixture of 2,4′-dimethyl-4-(*N*-phenylamino)quinoline (**2**, 0.001 mol) and 2-chloro-8-methylquinoline-3-carboxylic acid (0.0011 mol) was added to polyphosphoric acid (1 g of P_2O_5 and 0.5 mL H_3PO_4) and heated at 160 °C for 8 h. The reaction mixture showed two spots on TLC, and after the completion of the reaction the reaction mixture was poured into ice water, neutralized with saturated sodium bicarbonate solution to remove the excess of 2-chloro-8-methylquinoline-3-carboxylic acid, and extracted with ethyl acetate. The two products were separated using silica gel column chromatography. The first product **5** and the second product **6** were eluted with a petroleum ether : ethyl acetate (99 : 1) and a petroleum ether : ethyl acetate (95 : 5) mixture, respectively. Compounds **5** and **6** were recrystallized using ethanol and methanol, respectively.

*2,6,9-Trimethyl-7-(2-chloro-8-methylquinolin-3-yl)dibenzo [b,h][1,6]naphthyridine (**5a**)*

M. p. 210 – 212 °C. – Yield: 0.118 g (35 %). – IR (KBr): ν = 1628 and 1611 (C=N), 1590, 1561 cm^{-1}. – ^1H NMR (400 MHz, $CDCl_3$): δ = 2.56 (s, 3 H, 9-CH_3), 2.70 (s, 3 H, 2-CH_3), 2.81 (s, 3 H, 8′-CH_3), 3.14 (s, 3 H, 6-CH_3) 7.46 – 7.78 (m, 7 H, 3-H, 4-H, 8-H, 10-H, 5′-H, 6′-H, 7′-H), 8.08 (s, 1 H, 4′-H), 8.21 (d, J = 8.54 Hz, 1 H, 11-H), 9.17 (s, 1 H, 1-H). – ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.77 (9-CH_3), 22.30 (2-CH_3), 22.83 (8′-CH_3), 30.14 (6-CH_3), 118.13 (C-7a), 121.31 (C-6a), 122.48 (C-8), 127.15 (C-7), 127.55 (C-1), 128.07 (C-5′), 128.52 (C-9), 128.82 (C-6′), 129.06 (C-7′), 129.18 (C-3), 129.93 (C-4), 130.40 (C-3′), 131.35 (C-10), 133.74 (C-11), 134.20 (C-2), 134.32 (C-8′), 134.88 (C-4′), 139.25 (C-12b), 142.33 (C-11a), 146.42 (C-4′a), 147.36 (C-8′a), 147.66 (C-4a), 148.37 (C-12a), 152.45 (C-2′), 158.69 (C-6). – MS (EI, 70 eV): *m/z* (%) = 449/447 (28/91) [M+2]/$[M]^+$. – $C_{29}H_{22}N_3Cl$ (447.96): calcd. C 77.85, H 4.92, N 9.39; found C 78.02, H 4.64, N 9.17.

*2,6,9-Trimethyl-7-(8-methylquinolin-2[1H]-on-3-yl)dibenzo [b,h][1,6]naphthyridine (**6a**)*

M. p. 265 – 267 °C. – Yield: 0.073 g (17 %). – IR (KBr): ν = 1649 (C=O), 1623 and 1602 (C=N), 1592 cm^{-1}. – ^1H NMR (400 MHz, $CDCl_3$): δ = 2.50 (s, 3 H, 9-CH_3), 2.69 (s, 3 H, 2-CH_3), 2.80 (s, 3 H, 8′-CH_3), 3.09 (s, 3 H, 6-CH_3) 7.44 – 7.70 (m, 7 H, 3-H, 4-H, 8-H, 10-H, 5′-H, 6′-H, 7′-H), 7.94 (s, 1 H, 4′-H), 8.28 (d, 1 H, J = 8.54 Hz, 11-H), 9.23 (s, 1 H, 1-H) 9.29 (b s, 1H, N-1-H of quinoline). – ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.77 (9-CH_3), 22.30 (2-CH_3), 22.85 (8′-CH_3), 30.17 (6-CH_3), 118.16 (C-7a), 121.34 (C-6a), 122.49 (C-8), 127.19 (C-7), 127.56 (C-1), 128.11 (C-5′), 128.52 (C-9), 128.84 (C-6′), 129.07 (C-7′), 129.18 (C-3), 129.93 (C-4), 130.52 (C-3′), 131.35 (C-10), 133.74 (C-11), 134.21 (C-2), 134.36 (C-8′), 135.03 (C-4′), 139.25 (C-12b), 142.33 (C-11a), 146.44 (C-4′a), 147.40 (C-8′a), 147.66 (C-4a), 148.37 (C-12a), 158.71 (C-6), 170.02 (2′-C=O). – MS (EI, 70 eV): *m/z* (%) = 429 (89) $[M]^+$. – $C_{29}H_{23}N_3O$ (429.51): calcd. C 81.12, H 5.36, N 9.79; found C 81.08, H 5.12, N 9.69.

*4,6,9-Trimethyl-7-(2-chloro-8-methylquinolin-3-yl)dibenzo [b,h][1,6]naphthyridine (**5b**)*

M. p. 206 – 208 °C. – Yield: 0.125 g (28 %). – IR (KBr): ν = 1627 and 1608 (C=N), 1592, 1570 cm^{-1}. – ^1H NMR (400 MHz, $CDCl_3$): δ = 2.58 (s, 3 H, 9-CH_3), 2.74 (s, 3 H, 4-CH_3), 2.84 (s, 3 H, 8′-CH_3), 3.12 (s, 3 H, 6-CH_3) 7.51 – 7.73 (m, 7 H, 2-H, 3-H, 8-H, 10-H, 5′-H, 6′-H, 7′-H), 8.03 (s, 1 H, 4′-H), 8.19 (d, 1 H, J = 8.70 Hz, 11-H), 9.10 (d, 1 H, J = 7.82 Hz, 1-H). – ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.77 (9-CH_3), 22.41 (4-CH_3), 22.83 (8′-CH_3), 30.16 (6-CH_3), 118.13 (C-7a), 121.31 (C-6a), 122.48 (C-8), 127.15 (C-7), 127.48 (C-1), 128.07 (C-5′), 128.52 (C-9), 128.82 (C-6′), 129.06 (C-7′), 129.10 (C-2), 129.33 (C-3), 130.40 (C-3′), 131.35 (C-10), 133.74 (C-11), 134.32 (C-4), 134.41 (C-8′), 134.88 (C-4′), 139.28 (C-12b), 142.33 (C-11a), 146.42 (C-4′a), 147.36 (C-8′a), 147.73 (C-4a), 148.40 (C-12a), 152.45 (C-2′), 158.71 (C-6). – MS (EI, 70 eV): *m/z* (%) = 449/447 (34/100) [M+2]/$[M]^+$. – $C_{29}H_{22}N_3Cl$ (447.96): calcd. C 77.85, H 4.92, N 9.39; found C 77.71, H 4.69, N 9.21.

*4,6,9-Trimethyl-7-(8-methylquinolin-2[1H]-on-3-yl)dibenzo [b,h][1,6]naphthyridine (**6b**)*

M. p. 260 – 262 °C. – Yield: 0.064 g (15 %). – IR (KBr): ν = 1642 (C=O), 1626 and 1598 (C=N), 1580 cm^{-1}. – ^1H NMR (400 MHz, $CDCl_3$): δ = 2.48 (s, 3 H, 9-CH_3), 2.71 (s, 3 H, 4-CH_3), 2.82 (s, 3 H, 8′-CH_3), 3.11 (s, 3 H, 6-CH_3) 7.47 – 7.72 (m, 7 H, 2-H, 3-H, 8-H, 10-H, 5′-H, 6′-H, 7′-H), 7.97 (s, 1H, 4′-H), 8.29 (d, J = 8.70 Hz, 1 H, 11-H), 9.21 (dd, J = 7.90, 1.18 Hz, 1H, 1-H), 9.36 (b s, 1H, N-1-H of quinoline). – ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.77 (9-CH_3), 22.30 (4-CH_3), 22.85 (8′-CH_3), 30.18 (6-CH_3), 118.16 (C-7a), 121.34 (C-6a), 122.49 (C-8), 127.19 (C-7), 127.49 (C-1), 128.07 (C-5′), 128.52 (C-9), 128.82 (C-6′), 129.06 (C-7′), 129.10 (C-2), 129.33 (C-3), 130.52 (C-3′), 131.35 (C-10), 133.74 (C-11), 134.32 (C-4), 134.41 (C-8′), 135.03 (C-4′), 139.28 (C-12b), 142.33 (C-11a), 146.44 (C-4′a), 147.40 (C-8′a), 147.73 (C-4a), 148.40 (C-12a), 158.72 (C-6), 169.88 (2′-C=O). – MS (EI, 70 eV): *m/z* (%) = 429 (98) $[M]^+$. – $C_{29}H_{23}N_3O$ (429.51): calcd. C 81.12, H 5.36, N 9.79; found C 81.18, H 5.31, N 10.01.

*2-Chloro-6,9-dimethyl-7-(2-chloro-8-methylquinolin-3-yl) dibenzo[b,h][1,6]naphthyridine (**5c**)*

M. p. 215 – 217 °C. – Yield: 0.112 g (24 %). – IR (KBr): ν = 1628 and 1606 (C=N), 1590, 1538 cm^{-1}. – ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.59 (s, 3 H, 9-CH_3), 2.73 (s, 3 H, 8′-CH_3), 2.80 (s, 3 H, 6-CH_3) 7.42 – 7.71 (m, 7 H, 3-H, 4-H, 8-H, 10-H, 5′-H, 6′-H, 7′-H), 8.06 (s, 1 H, 4′-H), 8.17 (d,, J = 8.61 Hz, 1 H 11-H), 9.22 (s, 1 H, 1-H). – ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.77 (9-CH_3), 22.83 (8′-CH_3), 30.14 (6-CH_3), 118.13 (C-7a), 121.31 (C-6a), 122.48 (C-8), 127.15 (C-7), 127.53 (C-1), 128.07 (C-5′), 128.52 (C-9), 128.82 (C-6′), 129.06 (C-7′), 129.20 (C-3), 129.94 (C-4), 130.40 (C-3′), 131.35 (C-10), 133.74 (C-11), 134.17 (C-2), 134.32 (C-8′), 134.88 (C-4′), 139.25 (C-12b), 142.33 (C-11a), 146.42 (C-4′a), 147.36 (C-8′a), 147.66 (C-4a), 148.37 (C-12a), 152.45 (C-2′), 158.68 (C-6). – MS (EI, 70 eV): *m/z* (%) = 471/469/467 (32/59/98) [M+4]/[M+2]/$[M]^+$. – $C_{28}H_{19}N_3Cl_2$ (468.38): calcd. C 71.95, H 4.07, N 8.99; found C 71.78, H 3.88, N 8.54.

*2-Chloro-6,9-dimethyl-7-(8-methylquinolin-2[1H]-on-3-yl) dibenzo[b,h][1,6]naphthyridine (**6c**)*

M. p. 215 – 217 °C. – Yield: 0.054 g (12 %). – IR (KBr): ν = 1644 (C=O), 1624 and 1601 (C=N), 1588, 1540 cm^{-1}. – ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.51 (s, 3 H, 9-CH_3), 2.72 (s, 3 H, 8′-CH_3), 3.14 (s, 3 H, 6-CH_3) 7.46 – 7.81 (m, 7 H 3-H, 4-H, 8-H, 10-H, 5′-H, 6′-H, 7′-H), 7.93 (s, 1 H, 4′-H), 8.25 (d, J = 8.61 Hz, 1 H, 11-H), 9.24 (s, 1 H, 1-H), 9.33 (b s, 1H, N-1-H of quinoline). – ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.77 (9-CH_3), 22.85 (8′-CH_3), 30.17 (6-CH_3), 118.16 (C-7a), 121.34 (C-6a), 122.49 (C-8), 127.19 (C-7), 127.56 (C-1), 128.11 (C-5′), 128.52 (C-9), 128.84 (C-6′), 129.07 (C-7′), 129.18 (C-3), 129.93 (C-4), 130.52 (C-3′), 131.35 (C-10), 133.74 (C-11), 134.21 (C-2), 134.36 (C-8′), 135.03 (C-4′), 139.25 (C-12b), 142.33 (C-11a), 146.44 (C-4′a), 147.40 (C-8′a), 147.66 (C-4a), 148.37 (C-12a), 158.71 (C-6), 169.94 (2′-C=O). – MS (EI, 70 eV): *m/z* (%) = 451/449 (32/100) [M+2]/$[M]^+$. – $C_{28}H_{20}N_3ClO$ (449.50): calcd. C 74.83, H 4.45, N 9.35; found C 74.91, H 4.04, N 9.19.

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