# Synthesis of quinolino[2′,3′:7,6]cyclohept[*b*]indoles and their antimicrobial activities

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Practicable and concise syntheses of 6-chloro-7,8,9,14-tetrahydroquinolino[2′,3′:7,6]cyclohept[*b*]indoles by two routes are described. Both commenced with 1-oxo-2,3,4,5,10-hexahydrocyclohept[*b*]indoles and utilised either the acid-catalysed condensation with 2-aminobenzonitrile, followed by treatment with $POCl_3$ or, better, direct condensation of the ketone with anthranilic acid in $POCl_3$.

**Keywords:** 1-oxo-2,3,4,5,10-hexahydrocyclohept[*b*]indoles, 6-hydroxy-7,8,9,14-tetrahydroquinolino[2′,3′:7,6]cyclohept[*b*]indoles, 6-chloro-7,8,9,14-tetrahydroquinolino[2′,3′:7,6]cyclohept[*b*]indoles

Development of new methods for the synthesis of funtionalised indoles is currently attracting organic chemists due to the discovery of many indole alkaloids with varied biological activities.[1–6] The antidepressant activity of cyclohept[*b*]indole[7] has stimulated considerable interest and lead to the synthesis of large number of derivatives.[8–10] Indole-containing alkaloids such as prenylated indoles, carbazoles, indoloquinolines and cyclohept[*b*]indoles show biological activities such as anti-fungal, anti-bacterial, anti-tumour, anti-HIV, and DNA interaction properties.[11–14] Ervitsine and Ervatamine[15] are important members of a class of pyrido- fused cyclohept[*b*]indole alkaloids. Several methods have been reported[16–20] to construct this type of moiety, because of their important biological activities.[21–22] In this context, due to the promising pharmacological activity of some chlorinated indole derivatives we have devised a concise approach to 6-chloro-7,8,9,14-tetrahydroquinolino [2′,3′:7,6]cyclohept[*b*]indole derivatives which is based upon the Friedländer quinoline synthesis. We also report the antibacterial activities of the synthesised compounds.

To obtain our target compound, 1-oxocyclohept[*b*]indole **1** was chosen as a synthon, which underwent condensation with 2-aminobenzonitrile **2** under acid-catalysis using typical Friedländer conditions.[23,24] Thus, cycloheptindole **1a** on condensation with 2-aminobenzonitrile **2** in toluene in the presence of a catalytic amount of *p*-toluenesulfonic acid, gave a single product **3a**. The IR spectrum of this compound showed a strong absorption at 1650 $cm^{-1}$, ascribable to a C=O vibration. Two strong bands at 3359, 3238 $cm^{-1}$ were due to the presence of indole N–H and quinolone N–H groups respectively. The $^1H$ NMR spectrum exhibited a singlet at δ 2.41 for the C-11 methyl group, and three multiplets at δ 2.14–2.16, 2.85–2.87 and 3.04–3.08 for the C-8, C-7 and C-9 methylene protons respectively. The five aromatic protons (H-3, H-4, H-10, H-12 and H-13) absorbed in the region δ 7.13–7.85. Two deshielded doublets at δ 7.96 and 8.42 were assignable to H-5 and H-2 with *J* values of 7.9 Hz and 7.5 Hz respectively. A broad singlet at δ 11.43 was attributed to the indole NH proton. The OH proton resonated at δ 13.16 as a singlet. The $^{13}C$ spectrum of **3a** exhibited the presence of 21 carbon atoms. The IR and $^1H$ NMR spectra of compound **3a** revealed that it exists in the keto (quinolone) form in the solid phase and enolic (hydroxyquinoline) form in solution. In the mass spectrum, the molecular ion peak appeared at *m/z* 314 (25%). The elemental analysis also agreed well with the molecular formula, $C_{21}H_{18}N_2O$. On the basis of the spectroscopic data, the structure of the product was proved to be 6-hydroxy-11-methyl-7,8,9,14-tetrahydroquinolino[2′,3′:7,6]cyclohept[*b*]indole **3a**. A similar series of compounds **3b–e** were obtained from **1b–e** respectively.

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To synthesise 6-chloro-11-methyl-7,8,9,14-tetrahydroquinolino[2′,3′:7,6]cyclohept[*b*]indole **4a**, the 4-quinolone **3a** was refluxed with $POCl_3$ to give a single product, following aqueous work and column chromatography, in poor yield (22%). The disappearance of two prominent peaks at 1650 $cm^{-1}$ and 3238 $cm^{-1}$ and the presence of a C=N stretching band at 1589 $cm^{-1}$ in its IR spectrum revealed the formation of compound **4a**. In the $^1H$ NMR spectrum, a singlet at δ 13.16 disappeared and the remaining protons resonated in the corresponding aliphatic and aromatic regions. The presence of a chlorine atom was confirmed by a Lassaigne test and by the mass spectrum which showed a molecular ion $[M^+]$ at *m/z* 332 for $C_{21}H_{17}{}^{35}ClN_2$ and an (M+2) peak ($^{37}Cl$ isotope) at *m/z* 334. Furthermore, the $^{13}C$ NMR spectrum exhibited a signal at δ 140.72 due to the C-6-Cl carbon. All the spectral and analytical data established that the structure of the compound was 6-chloro-quinolino[2′,3′:7,6]cyclohept[*b*]indole **4a** (Scheme 1).

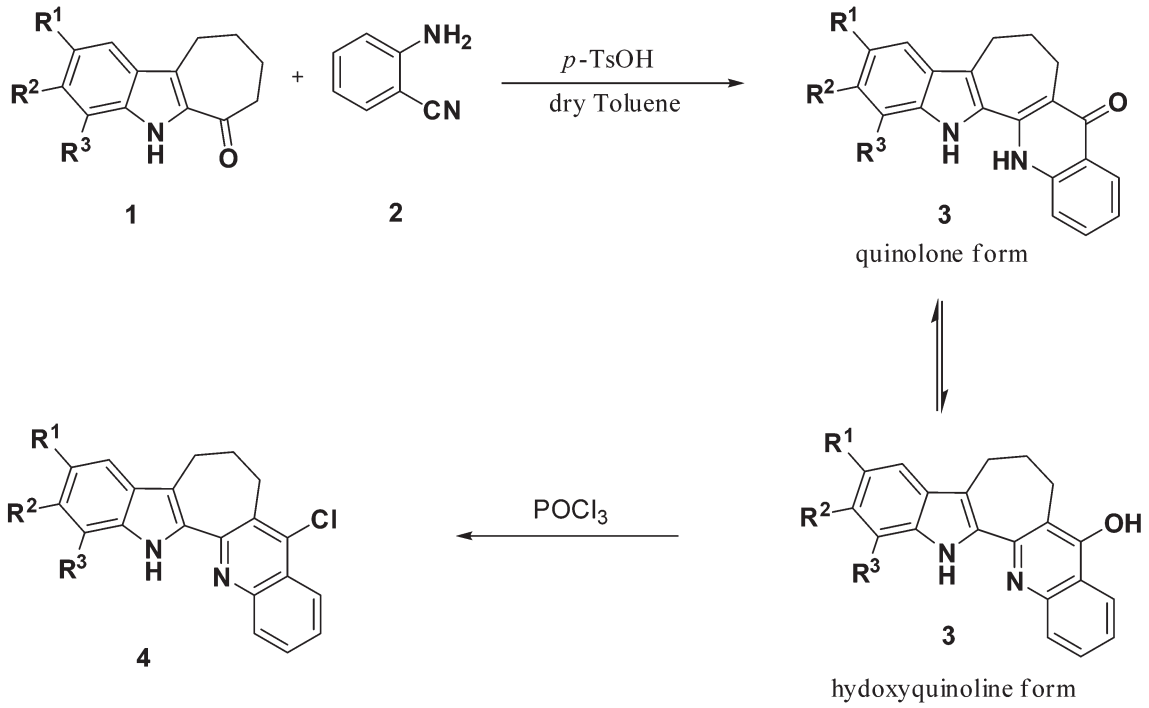
The yields from each step in the above route to 6-chloroquinolino[2′,3′:7,6]cyclohept[*b*]indole (**4**) were moderate (Table 1, method 1). So, in order to increase the yield of the target molecule, we designed an alternate method in which 1-oxocyclohept[*b*]indole **1a** was reacted with anthranilic acid. However, this reaction did not proceed under *p*-TsOH catalysis. When the same reactants were treated with phosphorous oxychloride at reflux temperature for 16 h the product, **4a** was obtained (Scheme 2) in satisfactory yield. From the TLC, mixed melting point and superimposable IR spectra, the compound was identical in all respects to that obtained from the two step sequence (Scheme 1). Overall, the yield of the final products was substantially better from the one pot synthesis. (Table 1, method 2)

The mechanism for the formation of 6-chloroquinolinocycloheptindole **4** from the condensation of 1-oxocyclohept [*b*]indole **1** with anthranilic acid in the presence of $POCl_3$ can be rationalised by invoking initial enamine formation followed by intramolecular cyclisation and subsequent halogen transfer.

*Antibacterial activity*

The antibacterial potency of compounds **3a–e** and **4a–e** were tested against six pathogenic bacteria by the agar well diffusion method and the minimal inhibitory concentration (MIC in μg $mL^{-1}$) was determined using this method. For comparison, different concentrations of oxytetracycline and kanamycin solutions were used as standards. The MIC was considered to be the lowest concentration of the tested compound which inhibited growth of bacteria on the plates. The diameter of the inhibition zones corresponding to the MICs are presented in Table 2.

From the analysis of Table 2, compound **4e** was found to be efficient in inhibiting the growth of bacteria when compared to




**1**, **2**, **3**, **4**

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

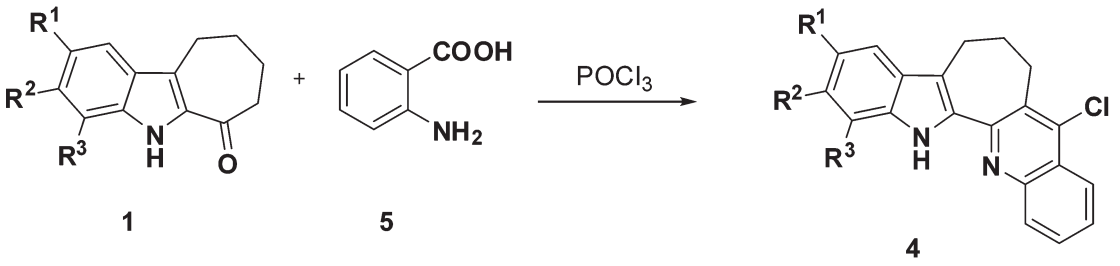
**Scheme 1**

**Table 1** Comparative yields of products

| Compounds | Yield /% | | | |
|---|---|---|---|---|
| | Method 1 | | | Method 2 |
| | Conversion of **1** to **3** | Conversion of **3** to **4** | Overall yield | One pot synthesis of **4** from **1** |
| **4a** | 42 | 20 | 8 | 38 |
| **4b** | 48 | 16 | 8 | 35 |
| **4c** | 44 | 18 | 8 | 39 |
| **4d** | 42 | 16 | 7 | 36 |
| **4e** | 40 | 20 | 8 | 38 |

other compounds tested. This may be due to the presence of the chlorine substituent. Also compound **3e** showed considerable activity, due to the presence of hydroxyl and chlorine groups. Some of the 6-hydroxy-7,8,9,14-tetrahydroquinolino [2′,3′:7,6]cyclohept[*b*]indoles **3** were found to have no activity towards *K. pneumonia, S. typhi*, or to *C. albicans*. In general, all the compounds tested have a high inhibiting activity towards bacteria.

In summary, a general and simple method for transformation of the cyclohept[*b*]indole **1** into 6-chloroquinolino[2′,3′: 7,6]cyclohept[*b*]indoles (**4**) in a one-pot synthesis has been described.




**1**, **5**, **4**

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

**Scheme 2**

**Table 2** Antibacterial activity of compounds **3** and **4**

| No. | Compounds | Bacteria MIC in μg mL$^{-1}$ (zone of inhibition in mm) | | | | | |
|---|---|---|---|---|---|---|---|
| | | *S. aureus* (NCIM5021) | *E. coli* (MTCC2109) | *K.pneumonia* (NCIM2957) | *P.aeruginosa* (NCIM2242) | *S. typhi* (MTCC135) | *C. albicans* (NCIM3471) |
| 1 | **3a** | 165 (6) | 155 (5) | 135 (6) | 165 (8) | Nil | Nil |
| 2 | **3b** | 150 (8) | 160 (7) | Nil | 155 (9) | Nil | 165 (6) |
| 3 | **3c** | 140 (5) | 185 (7) | Nil | 160 (8) | 190 (4) | 160 (6) |
| 4 | **3d** | 185 (9) | 165 (8) | Nil | 160 (6) | Nil | Nil |
| 5 | **3e** | 145 (11) | 150 (13) | 145 (11) | 155 (15) | 165 (13) | 155 (12) |
| 6 | **4a** | 135 (7) | 120 (8) | 145 (7) | 125 (6) | 140 (9) | 145 (8) |
| 7 | **4b** | 150 (11) | 135 (10) | 155 (9) | 140 (12) | 155 (13) | 125 (10) |
| 8 | **4c** | 140 (9) | 150 (14) | 135 (13) | 135 (15) | 145 (13) | 140 (14) |
| 9 | **4d** | 155 (10) | 145 (12) | 150 (11) | 145 (10) | 155 (12) | 155 (13) |
| 10 | **4e** | 130 (17) | 155 (15) | 160 (15) | 140 (18) | 140 (13) | 150 (15) |
| 11 | Oxytetracycline (150 μg mL$^{-1}$) | (22) | (19) | (20) | (22) | (17) | (21) |
| 12 | Kanamycin (150 μg mL$^{-1}$) | (24) | (20) | (25) | (26) | (21) | (23) |

MTCC, NCIM–Microbial type culture collection IMTECH, Chandigarh.

## Experimental

Melting points were determined on Mettler FP 51apparatus (Mettler Instruments, Switzerland) and are uncorrected. They are expressed in (°C). IR spectra were recorded on a Shimadzu FTIR-8201PC spectrophotometer (Shimadzu, Japan) using KBr discs. $^1$H NMR spectra ware recorded on Bruker AMX 400 (400 MHz) at IISc, Bangalore and on a Bruker AMX 500 (500 MHz) spectrometer at IIT, Chennai, using tetramethylsilane (TMS) as internal standard. The chemical shifts are expressed in parts per million (ppm). Microanalyses 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. 1-oxo-2,3,4,5,10-hexahydrocyclohept[*b*]indole was prepared by the reported procedure.[10] All chemicals were purchased from Aldrich, Bangalore, India.

For the *in vitro* evaluation of antibacterial activity the microorganism was suspended in sterile saline and diluted to $10^6$ cfu mL$^{-1}$. A solution of the synthesised compound (500 μg mL$^{-1}$) in water was prepared. The wells (8 mm in diameter) were cut from agar and 100 μL of solution was added to the well. After incubation for 24 h at 37 °C, all of the plates were examined for any zones of growth inhibition, and the diameter of the zones were measured in mm.

*Synthesis of 6-hydroxy-7,8,9,14-tetrahydroquinolino[2′,3′:7,6]cyclohept[b]indole* **(3)***; general procedure*

To a mixture of 1-oxo-2,3,4,5,10-hexahydrocyclohept[*b*]indole **1** (1 mmol) and 2-aminobenzonitrile (**2**, 0.118 g, 1 mmol) in dry toluene (10 mL) was added a catalytic amount of *p*-toluenesulfonic acid. The reaction mixture was refluxed in an oil-bath for 6 h. Completion of the reaction was checked by TLC. After all the starting materials had been consumed, the excess solvent was removed under reduced pressure and the mixture was poured into ice cold water. The resulting solid was filtered, dried and purified by column chromatography over silica gel using chloroform-methanol (9:1) as eluent to obtain the 6-hydroxy-7,8,9,14-tetra hydroquinolino[2′,3′:7,6]cyclohept[*b*]indole derivative (**3**).

*6-Hydroxy-11-methyl-7,8,9,14-tetrahydroquinolino[2′,3′:7,6]cyclohept[*b*]indole* **(3a):** Green solid, m.p. >300 °C. Yield: (131 mg, 42%). IR $\nu_{max}$ (cm$^{-1}$): 3359, 3238, 2921, 1650, 1578. $^1$H NMR (400 MHz, DMSO-$d_6$) δ: 2.14–2.16 (m, 2H, H-8), 2.41 (s, 3H, $CH_3$), 2.85–2.87 (m, 2H, H-7), 3.04–3.08 (m, 2H, H-9), 7.13 (d, 1H, *J* = 8.2 Hz, H-12), 7.41–7.43 (m, 2H, H-10, H-13), 7.58 (t, 1H, *J* = 7.9 Hz, H-4), 7.85 (t, 1H, *J* = 7.5 Hz, H-3), 7.96 (d, 1H, *J* = 7.9 Hz, H-5), 8.42 (d, 1H, *J* = 7.5 Hz, H-2), 11.43 (br. s, 1H, NH), 13.16 (s, 1H, OH). $^{13}$C NMR (100 MHz, DMSO-$d_6$) δ: 21.0 ($CH_3$), 21.6 (C-9), 24.1 (C-8), 28.1 (C-7), 111.0 (C-13), 112.4 (C-6a), 113.4 (C-5a), 114.9 (C-9a), 118.1 (C-10), 120.5 (C-12), 121.8 (C-5), 122.1 (C-4), 126.2 (C-2), 127.1 (C-9b), 128.7 (C-11), 129.1 (C-3), 132.3 (C-13a), 133.1 (C-14a), 144.9 (C-1a), 153.9 (C-14b), 172.1 (C-6). MS: *m/z* (%) 314 (M$^+$, 25), 313 (100), 312 (82), 298 (27), 293 (6), 269 (5), 181 (9), 156 (22), 149 (20), 115 (10), 77 (8), 43 (17). Anal. Calcd for $C_{21}H_{18}N_2O$: C, 80.25; H, 5.73; N, 8.91. Found: C, 80.16; H, 5.69; N, 8.93%.

*6-Hydroxy-12-methyl-7,8,9,14-tetrahydroquinolino[2′,3′:7,6]cyclohept[*b*]indole* **(3b):** Dark brown solid, m.p. >300 °C. Yield: (150 mg, 48%). IR $\nu_{max}$ (cm$^{-1}$): 3396, 3228, 2924, 1663, 1577. $^1$H NMR (400 MHz, DMSO-$d_6$) δ: 2.06–2.12 (m, 2H, H-8), 2.42 (s, 3H, $CH_3$), 2.92–2.96 (m, 2H, H-7), 3.07–3.11 (m, 2H, H-9), 6.83 (d, 1H, *J* = 8.0 Hz, H-11), 7.31 (s, 1H, H-13), 7.35 (t, 1H, *J* = 8.0 Hz H-4), 7.41 (d, 1H, *J* = 8.0 Hz, H-10), 7.59 (t, 1H, *J* = 8.1 Hz, H-3), 7.86 (d, 1H, *J* = 8.0 Hz, H-5), 8.20 (d, 1H, *J* = 8.1 Hz, H-2), 10.89 (br. s, 1H, NH), 13.01 (s, 1H, OH). $^{13}$C NMR (100 MHz, DMSO-$d_6$) δ: 20.9 ($CH_3$), 21.3 (C-9), 24.33 (C-8), 27.8 (C-7), 111.3 (C-13), 112.6 (C-6a), 113.4 (C-9a), 114.1 (C-5a), 119.6 (C-10), 120.8 (C-9b), 120.9 (C-5), 121.7 (C-4), 122.7 (C-11), 125.6 (C-2), 128.9 (C-3), 132.0 (C-13), 133.8 (C-14a), 135.8 (C-13a), 143.9 (C-1a), 154.1 (C-14b), 171.8 (C-6). MS: *m/z* (%) 314 (M$^+$, 32), 313 (100), 312 (68), 298 (20), 293 (7), 181 (12), 156 (20), 149 (15), 115 (5), 77 (9), 43 (14). Anal. Calcd for $C_{21}H_{18}N_2O$: C, 80.25; H, 5.73; N, 8.91. Found: C, 80.21; H, 5.65; N, 8.88%.

*6-Hydroxy-13-methyl-7,8,9,14-tetrahydroquinolino[2′,3′:7,6]cyclohept[*b*]indole* **(3c):** Green solid, m.p. 273 °C. Yield: (138 mg, 44%). IR $\nu_{max}$ (cm$^{-1}$): 3365, 3229, 2924, 1644, 1580. $^1$H NMR (400 MHz, DMSO-$d_6$) δ: 2.15–2.22 (m, 2H, H-8), 2.59 (s, 3H, $CH_3$), 2.83–2.90 (m, 2H, H-7), 3.04–3.12 (m, 2H, H-9), 7.04 (t, 1H, *J* = 7.8 Hz, H-11), 7.12 (d, 1H, *J* = 7.7 Hz, H-12), 7.51 (d, 1H, *J* = 7.8 Hz, H-10), 7.62 (t, 1H, *J* = 8.0 Hz, H-4), 7.89 (t, 1H, *J* = 8.1 Hz, H-3), 8.02 (d, 1H, *J* = 8.0 Hz, H-5), 8.46 (d, 1H, *J* = 8.1 Hz, H-2), 11.38 (br. s, 1H, NH), 13.18 (s, 1H, OH). $^{13}$C NMR (100 MHz, DMSO-$d_6$) δ: 17.2 ($CH_3$), 21.2 (C-9), 24.3 (C-8), 28.0 (C-7), 112.4 (C-6a), 113.5 (C-10), 113.6 (C-5a), 115.8 (C-9a), 117.5 (C-12), 120.5 (C-11), 121.9 (C-5), 123.7 (C-4), 125.6 (C-2), 126.1 (C-9b), 128.1 (C-3), 132.9 (C-14a), 138.6 (C-13a), 145.3 (C-1a), 154.7 (C-14b), 172.0 (C-6). MS: *m/z* (%) 314 (M$^+$, 27), 313 (100), 312 (76), 310 (10), 298 (15), 297 (11), 269 (8), 181 (14), 156 (8), 155 (14), 149 (18), 115 (13), 77 (12), 43 (21). Anal. Calcd for $C_{21}H_{18}N_2O$: C, 80.25; H, 5.73; N, 8.91. Found: C, 80.32; H, 5.71; N, 8.92%.

*6-Hydroxy-7,8,9,14-tetrahydroquinolino[2′,3′:7,6]cyclohept[*b*]indole* **(3d):** Green solid, m.p. >300 °C. Yield: (126 mg, 42%). IR $\nu_{max}$ (cm$^{-1}$): 3361, 3227, 2922, 1664, 1577. $^1$H NMR (400 MHz, DMSO-$d_6$) δ: 2.10–2.16 (m, 2H, H-8), 2.88–2.91 (m, 2H, H-7), 3.08–3.11 (m, 2H, H-9), 7.05 (t, 1H, *J* = 7.8 Hz, H-11), 7.23 (t, 1H, *J* = 7.7 Hz, H-12), 7.52 (d, 1H, *J* = 7.8 Hz, H-10), 7.60 (d, 1H, *J* = 7.7 Hz, H-13) 7.74 (t, 1H, *J* = 7.8 Hz, H-4), 7.81 (t, 1H, *J* = 7.7 Hz, H-3), 7.92 (d, 1H, *J* = 7.8 Hz, H-5), 8.34 (d, 1H, *J* = 7.7 Hz, H-2), 11.35 (br. s, 1H, NH), 13.20 (s, 1H, OH). $^{13}$C NMR (100 MHz, DMSO-$d_6$) δ: 22.0 (C-9), 24.8 (C-8), 28.6 (C-7), 112.1 (C-13), 112.8 (C-6a), 113.7 (C-5a), 113.9 (C-9a), 118.6 (C-10), 119.8 (C-11), 120.1 (C-12), 120.9 (C-5), 121.8 (C-4), 124.8 (C-9b), 127.1 (C-2), 128.7 (C-3), 134.1 (C-14a), 136.2 (C-13a), 143.9 (C-1a), 154.0 (C14-b), 172.1 (C-6). MS: *m/z* (%) 300 (M$^+$, 24), 299 (100), 298 (12), 283 (10), 257 (8), 231 (5), 195 (11), 181 (6), 157 (8), 115 (10), 77 (7), 43 (21). Anal. Calcd for $C_{20}H_{16}N_2O$: C, 80.00; H, 5.33; N, 9.33. Found: C, 79.92; H, 5.29; N, 9.28%.

*6-Hydroxy-11-chloro-7,8,9,14-tetrahydroquinolino[2′,3′:7,6]cyclohept[*b*]indole* **(3e):** Dark yellow solid, m.p. >300 °C. Yield: (133 mg, 40%). IR $\nu_{max}$ ($cm^{-1}$): 3368, 3245, 2923, 1646, 1577. $^1$H NMR (400 MHz, DMSO-$d_6$) δ: 2.17–2.21 (m, 2H, H-8), 2.82–2.85 (m, 2H, H-7), 3.04–3.07 (m, 2H, H-9), 7.33 (d d, 1H, $J_m$ = 1.9 Hz, $J_o$ = 8.7 Hz, H-12), 7.56 (d, 1H, $J$ = 8.7 Hz, H-13), 7.66 (t, 1H, $J$ = 8.0 Hz, H-4,), 7.78 (d, 1H, $J_m$ = 1.9 Hz, H-10), 7.93 (t, 1H, $J$ = 8.2 Hz, H-3), 7.98 (d, 1H, $J$ = 8.0 Hz H-5), 8.49 (d, 1H, $J$ = 8.2 Hz, H-2), 11.90 (br. s, 1H, NH), 13.30 (s, 1H, OH). $^{13}$C NMR (100 MHz, DMSO-$d_6$) δ: 22.7 (C-9), 23.8 (C-8), 28.1 (C-7), 112.1 (C-6a), 113.4 (C-5a), 113.9 (C-13), 114.1 (C-9a), 120.1 (C-10), 120.4 (C-5), 121.8 (C-4), 122.4 (C-12), 124.8 (C-11), 126.9 (C-2), 128.1 (C-3), 128.8 (C-9b), 134.2 (C-13a), 136.1 (C-14a), 144.0 (C-1a), 153.8 (C-14b), 171.9 (C-6). MS: *m/z* (%) 334 (100) [M+], 336 (M+2) (31), 334 ($M^+$, 24), 333 (8), 317 (15), 298 (36), 297 (40), 291 (16), 229 (6), 215 (8), 181 (17), 157 (8), 77 (5), 43 (12). Anal. Calcd for $C_{20}H_{15}ClN_2O$: C, 71.75; H, 4.52; N, 8.37. Found: C, 71.79; H, 4.52; N, 8.39%.

*One-pot synthesis of 6-chloro-7,8,9,14-tetrahydro quinolino[2′,3′:7,6] cyclohept[b]indoles* **(4)** *from 6-hydroxy-7,8,9,14-tetrahydro quinolino [2′,3′:7,6]cyclohept[b]indoles* **(3)***; general procedure*

A mixture of the appropriate 6-hydroxy-7,8,9,14-tetrahydroquinolino [2′,3′:7,6]cyclohept[*b*]indole derivative (**3**, 1 mmol) in phosphorous oxychloride (10 mL) was refluxed for 12 h. The reaction was monitored by TLC. After completion, the reaction mixture was poured into ice water with constant stirring and the pH was adjusted to 8 by addition of 10% NaOH solution. The precipitate formed was filtered off and dried. The crude product thus obtained was purified by column chromatography over silica gel using petroleum ether–ethyl acetate (99:1) as eluent to provide the corresponding 6-chloro-7,8,9,14-tetrah ydroquinolino[2′,3′:7,6]cyclohept [*b*]indole (**4**).

*6-Chloro-11-methyl-7,8,9,14-tetrahydroquinolino[2′,3′:7,6]cyclohept[*b*]indole* **(4a):** Yellow solid, m.p. 178 °C. Yield: (66 mg, 20%). IR $\nu_{max}$ ($cm^{-1}$): 3392, 2926, 1589. $^1$H NMR (500 MHz, $CDCl_3$) δ: 2.22–2.27 (m, 2H, H-8), 2.50 (s, 3H, $CH_3$), 3.23–3.26 (m, 2H, H-7), 3.42–3.44 (m, 2H, H-9), 7.15 (dd, 1H, $J_m$ = 1.5 Hz, $J_o$ = 8.2 Hz, H-12), 7.37 (d, 1H, $J$ = 8.2 Hz, H-13), 7.42 (d, 1H, $J$ = 1.5 Hz, H-10), 7.58 (dt, 1H, $J_m$ = 1.5 Hz, $J_o$ = 8.2 Hz, H-4), 7.72 (dt, 1H, $J_m$ = 1.5 Hz, $J_o$ = 8.0 Hz, H-3), 8.08 (dd, 1H, $J_m$ = 1.5 Hz, $J_o$ = 8.2 Hz, H-5), 8.22 (dd, 1H, $J_m$ = 1.5 Hz, $J_o$ = 8.0 Hz, H-2), 9.72 (br. s, 1H, NH). $^{13}$C NMR (125 MHz, $CDCl_3$) δ: 21.4 ($CH_3$), 27.8 (C-9), 24.2 (C-8), 29.8 (C-7), 110.7 (C-13), 111.0 (C-9a), 117.7 (C-10), 120.1 (C-5a), 120.2 (C-12), 124.7 (C-5), 126.1 (C-4), 126.5 (C-9b), 127.5 (C-11), 128.1 (C-6a), 129.1 (C-11a), 129.2 (C-2), 131.7 (C-3), 133.5 (C-13a), 140.7 (C-6), 146.4 (C-1a), 150.4 (C-14b). MS: *m/z* (%) 332 (100) [$M^+$], 334 (31) (M+2), 317 (20), 297 (12), 296 (22), 209 (7), 195 (5), 157 (12), 143 (8), 129 (10), 97 (7). Anal. Calcd for $C_{21}H_{17}ClN_2$: C, 75.78; H, 5.15; N, 8.42. Found: C, 75.67; H, 5.11; N, 8.39%.

*6-Chloro-12-methyl-7,8,9,14-tetrahydroquinolino[2′,3′:7,6]cyclohept[*b*]indole* **(4b):** Light yellow solid, m.p. 155 °C. Yield: (53 mg, 16%). IR $\nu_{max}$ ($cm^{-1}$): 3390, 2925, 1586. $^1$H NMR (400 MHz, $CDCl_3$) δ: 2.12–2.18 (m, 2H, H-8), 2.43 (s, 3H, $CH_3$), 3.14–3.17 (m, 2H, H-7), 3.32–3.34 (m, 2H, H-9), 6.88 (d d, 1H, $J_m$ = 1.0 Hz, $J_o$ = 8.0 Hz, H-11), 7.16 (s, 1H, H-13), 7.42 (d, 1H, $J$ = 8.0 Hz, H-10), 7.47 (dt, 1H, $J_m$ = 1.2 Hz, $J_o$ = 8.1 Hz, H-4), 7.62 (dt, 1H, $J_m$ = 1.2 Hz, $J_o$ = 8.1 Hz, H-3), 7.97 (dd, 1H, $J_m$ = 1.2 Hz, $J_o$ = 8.1 Hz, H-5), 8.13 (dd, 1H, $J_m$ = 1.2 Hz, $J_o$ = 8.1 Hz, H-2), 9.57 (br. s, 1H, NH). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 21.1 ($CH_3$), 24.8 (C-8), 27.4 (C-9), 29.7 (C-7), 111.1 (C-9a), 111.4 (C-13), 118.2 (C-10), 120.2 (C-5a), 121.6 (C-9b), 124.6 (C-5), 126.4 (C-4), 128.3 (C-6a), 129.2 (C-2), 129.3 (C-14a), 131.2 (C-12), 131.6 (C-3), 136.1 (C-13a), 140.1 (C-6), 146.7 (C-1a), 150.2 (C-14b). MS: *m/z* (%) 332 (100) [$M^+$], 334 (31) (M+2), 317 (14), 297 (18), 296 (28), 209 (5), 195 (10), 157 (8), 129 (15), 97 (10), 77 (11). Anal. Calcd for $C_{21}H_{17}ClN_2$: C, 75.78; H, 5.15; N, 8.42. Found: C, 75.75; H, 5.08; N, 8.46%.

*6-Chloro-13-methyl-7,8,9,14-tetrahydroquinolino[2′,3′:7,6]cyclohept[*b*]indole* **(4c):** White solid, m.p. 142 °C. Yield: (59 mg, 18%). IR $\nu_{max}$ ($cm^{-1}$): 3440, 2964, 1592. $^1$H NMR (500 MHz, $CDCl_3$) δ: 2.23–2.27 (m, 2H, H-8), 2.64 (s, 3H, $CH_3$), 3.26–3.28 (m, 2H, H-7), 3.34–3.42 (m, 2H, H-9), 7.08 (t, 1H, $J$ = 7.8 Hz, H-11), 7.14 (d, 1H, $J$ = 7.8 Hz, H-12), 7.50 (d, 1H, $J$ = 7.8 Hz, H-10), 7.58 (t, 1H, $J$ = 8.0 Hz, H-4), 7.73 (t, 1H, $J$ = 8.0 Hz, H-3), 8.12 (d, 1H, $J$ = 8.0 Hz, H-5), 8.24 (d, 1H, $J$ = 8.0 Hz, H-2), 9.70 (br. s, 1H, NH). $^{13}$C NMR (125 MHz, $CDCl_3$) δ: 16.8 ($CH_3$), 24.2 (C-8), 27.4 (C-9), 29.9 (C-7), 111.1 (C-9a), 117.3 (C-10), 119.3 (C-13), 119.7 (C-12), 120.5 (C-5a), 124.7 (C-11), 124.8 (C-5), 125.2 (C-9b), 126.8 (C-4), 128.9 (C-6a), 129.0 (C-14a), 129.5 (C-2), 131.9 (C-3), 135.7 (C-13a), 140.1 (C-6), 146.5 (C-1a), 150.9 (C-14b). MS: *m/z* (%) 332 (100) [$M^+$], 334 (32) (M+2), 317 (30), 297 (10), 296 (27), 209 (16), 195 (7), 157 (6), 143 (10), 129 (5), 97 (11), 77 (9). Anal. Calcd for $C_{21}H_{17}ClN_2$: C, 75.78; H, 5.15; N, 8.42. Found: C, 75.82; H, 5.05; N, 8.44%.

*6-Chloro-7,8,9,14-tetrahydroquinolino[2′,3′:7,6]cyclohept[*b*]indole* **(4d):** Light yellow solid, m.p. 133 °C. Yield: (50 mg, 16%). IR $\nu_{max}$ ($cm^{-1}$): 3431, 2963, 1585. $^1$H NMR (400 MHz, $CDCl_3$) δ: 2.21–2.26 (m, 2H, $C_8$-2H), 3.24–3.27 (m, 2H, $C_7$-2H), 3.40–3.43 (m, 2H, $C_9$-2H), 7.12 (dt, 1H, $J_m$ = 1.0 Hz, $J_o$ = 7.8 Hz, H-11), 7.29 (dt, 1H, $J_m$ = 1.0 Hz, $J_o$ = 8.0 Hz, H-12), 7.44 (d, 1H, $J$ = 8.0 Hz, H-13), 7.56 (dt, 1H, $J_m$ = 1.6 Hz, $J_o$ = 7.9 Hz, H-4), 7.62 (dd, 1H, $J_m$ = 1.0 Hz, $J_o$ = 7.8 Hz, H-10), 7.70 (dt, 1H, $J_m$ = 1.6 Hz, $J_o$ = 8.0 Hz, H-3), 8.05 (d, 1H, $J$ = 7.9 Hz, H-5), 8.21 (dd, 1H, $J_m$ = 1.6 Hz, $J_o$ = 8.0 Hz, H-2), 9.78 (b s, 1H, NH). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 25.1 (C-8), 26.4 (C-9), 29.6 (C-7), 110.7 (C-9a), 111.4 (C-13), 118.7 (C-10), 119.6 (C-11), 121.1 (C-12), 121.4 (C-5a), 124.1 (C-5), 124.2 (C-9b), 126.7 (C-4), 128.1 (C-2), 129.1 (C-14a), 129.1 (C-6a), 132.2 (C-3), 136.5 (C-13a), 141.1 (C-6), 146.3 (C-1a), 150.1 (C-14a). MS: *m/z* (%) 332 (100) [$M^+$], 334 (31) (M+2), 317 (24), 283 (15), 282 (28), 257 (8), 231 (7), 143 (16), 129 (10), 91 (8), 77 (12). Anal. Calcd for $C_{20}H_{15}ClN_2$: C, 75.35; H, 4.74; N, 8.79. Found: C, 75.30; H, 4.72; N, 8.85%.

*6,11-Dichloro-7,8,9,14-tetrahydroquinolino[2′,3′:7,6]cyclohept[*b*] indole* **(4e):** Yellow solid, m.p. 163 °C. Yield: (70 mg, 20%). IR $\nu_{max}$ ($cm^{-1}$): 3430, 2963, 1586. $^1$H NMR (400 MHz, $CDCl_3$) δ: 2.16–2.23 (m, 2H, H-8), 3.15–3.18 (m, 2H, H-7), 3.37–3.40 (m, 2H, H-9), 7.22 (dd, 1H, $J_m$ = 2.0 Hz, $J_o$ = 8.4 Hz, H-12), 7.34 (d, 1H, $J$ = 8.4 Hz, H-13), 7.44–7.58 (m, 2H, H-4, H-10), 7.69 (dt, 1H, $J_m$ = 1.6 Hz, $J_o$ = 8.0 Hz, H-3), 8.04 (d, 1H, $J$ = 8.2 Hz, H-5), 8.20 (dd, 1H, $J_m$ = 1.6 Hz, $J_o$ = 8.0 Hz, H-2), 9.81 (br. s, 1H, NH). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 25.2 (C-8), 26.9 (C-9), 29.8 (C-7), 110.9 (C-9a), 114.1 (C-13), 120.1 (C-5a), 120.3 (C-10), 121.6 (C-12), 124.4 (C-5), 125.7 (C-11), 126.2 (C-4), 127.8 (C-6a), 128.8 (C-9b), 129.5 (C-2), 130.9 (C-3), 134.2 (C-13a), 139.9 (C-6), 147.1 (C-1a), 151.0 (C-14b). MS: *m/z* (%) 352 (100) [$M^+$], 354 (64) (M+2), 351 (34), 317 (18), 316 (30), 291 (8), 282 (14), 241 (5), 227 (6), 215 (10), 177 (17), 149 (7), 111 (9). Anal. Calcd for $C_{20}H_{14}Cl_2N_2$: C, 68.00; H, 3.99; N, 7.93. Found: C, 68.12; H, 4.02; N, 7.94%.

*Synthesis of 6-chloro-7,8,9,14-tetrahydroquinolino [2′,3′:7,6]cyclohept[b]indoles* **(4)** *from 1-oxo-2,3,4,5,10-hexahydrocyclohept[b] indole (***1***); general procedure*

A mixture of 1-oxo-2,3,4,5,10-hexahydrocyclohept[*b*]indole **1** (1 mmol), anthranilic acid (0.137 g, 1 mmol) in phosphorous oxychloride (20 mL) was refluxed at 130 ºC for 18 h. After completion of the reaction, the mixture was poured into ice water. The pH of the solution was adjusted to 8 by addition of 10% NaOH solution. The precipitate formed was filtered off and dried. The crude product thus obtained was purified by column chromatography over silica gel using petroleum ether-ethyl acetate (99:1) as eluent to yield the corresponding 6-chloro-7,8,9,14-tetrahydroquinolino[2′,3′:7,6]cyclohept[*b*]indole (**4**).

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