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# Microwave-assisted synthesis of some new biquinoline compounds catalyzed by DMAP and their biological activities

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A series of new biquinoline compounds **4a-t** have been synthesized by reaction of [(2-chloro-3-quinolyl) methylene]methane-1,1-dicarbonitrile **2a-d** and 3-arylamino-5,5-dimethyl-cyclohex-2-en-1-one **3a-e** under microwave irradiation catalyzed by 4-(N,N-dimethylamino) pyridine (DMAP). This newer method produces pure product in high yield rapidly. The synthesized compounds **4a-t** have been characterized by elemental analysis, IR, NMR and screened for their antifungal and antibacterial activity.

**Keywords**: Biquinoline, DMAP, microwave heating, microbial activity

Microwave-assisted synthesis has attracted a considerable amount of attention in recent years and has been applied successfully for the preparation of biologically active heterocycles[1-4]. The main benefits of performing reactions under microwave irradiation conditions are the significant rate-enhancements and the higher product yields observed.

In recent times, the use of 4-dimethyl amino pyridine[5] has received considerable attention as an inexpensive, readily available catalyst.

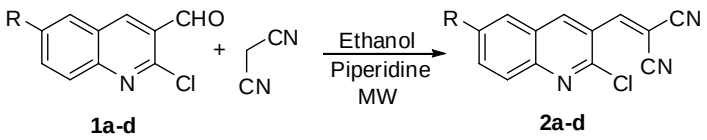
The quinolines and their derivatives are known to possess useful biological activities such as anti-malarial[6], anti-inflammatory[7], bactericidal[8], fungi-cidal[9], anticancer[10], *etc*. Because of their important role in the pharmaceutical field[11], significant effort continues to be directed into the development of new quinoline based structures and new methods for their preparation. Biquinoline compounds attract wide-spread interest due to their variety of applications[12-14] and therefore, various methods for the preparation of 2, 3′- (ref. 15), 2, 2′- (ref. 16), 8,8′- (ref. 17) 3,6′-and 3,7′- (ref. 18) biquinoline have been reported. To the extent of present knowledge, there is no report on synthesis of 4,3′-biquinoline using 2-chloro-3-formyl quinoline so far.

Encouraged by the importance of above mentioned heterocycles and as part of the research in the laboratory towards synthesis of biologically relevant heterocyclic compounds[19] herein is reported newer and more efficient methods to construct new 4,3′-biquinoline scaffold catalyzed by DMAP under microwave irradiation.

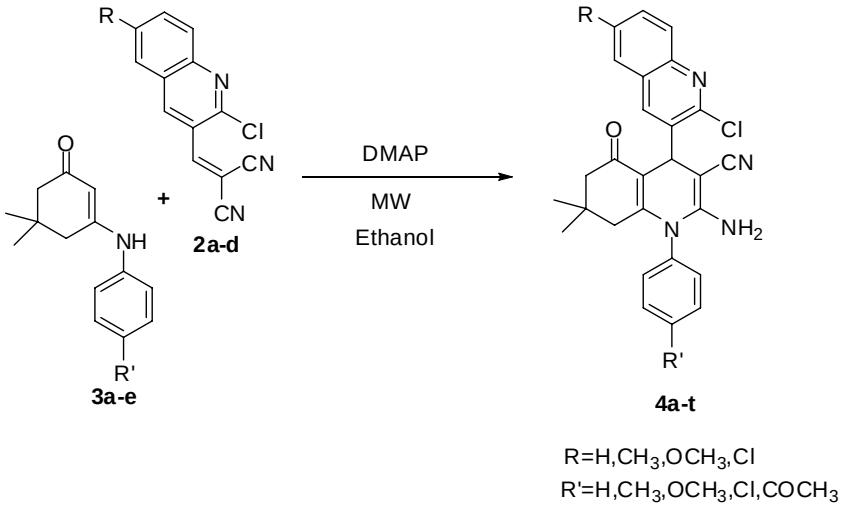
## Results and Discussion

In the present work, 2-chloro-3-formyl quinolines **1a-d** were prepared by known procedures given in the literature[20]. The compounds [(2-chloro-3-quinolyl) methylene] methane-1,1-dicarbonitrile **2a-d** were prepared by Knoevenagel condensations between malononitrile and 2-chloro-3-formyl quinoline **1a-d** in ethanol under microwave irradiation using a drop of piperidine as a catalyst in good yields **(Scheme I)**. The identity of the product was determined by IR and $^1$H NMR spectral studies. The IR spectrum exhibited a sharp band at 2215 cm$^{-1}$ confirming the presence of CN functionality. The $^1$H NMR spectra showed the absence of the aldehyde proton. Moreover, 3-aryl-amino-5,5-dimethyl-cyclohex-2-en-1-one **3a-e** were synthesized according to the literature[21] by microwave irradiation.

Various 3-arylamino-5,5-dimethyl-cyclohex-2-en-1-one **3a-e**, [(2-chloro-3-quinolyl)methylene]meth-ane-1,1-dicarbonitrile **2a-d** and catalytic amount of DMAP were subjected to microwave irradiation to produce corresponding biquinoline compound **(Scheme II)** in high yield as shown in the **Table I**. The structures of the compounds were confirmed on the basis of elemental analysis and spectral data. As an example, the IR spectrum of the compound **4k** showed bands at 3320 (asym. N-H str.) and 3250 cm$^{-1}$




**Scheme I**




**Scheme II**

(sym. N-H str.) for $-NH_2$, 2220 $cm^{-1}$ for CN and 1650 $cm^{-1}$ for C=O stretching. $^1$H NMR spectrum of **4k** showed singlets at δ 0.93 and 0.97 for two methyl group and multiplet of two methylene group at δ 1.69-2.20. The singlets at δ 4.18 and 5.17 appeared for amine and methine group respectively. A multiplet due to the aromatic protons appeared at δ 7.08-8.15. The $^{13}$C NMR spectrum of **4k** was in good agreement with the structure assigned. The peaks at δ 27.32 and 29.41 are assigned to two methyl carbons, the peaks at δ 32.19 and 37.93 are assigned to two methylene carbons and peaks at δ 55.63 and 55.73 attributed to two methoxy carbons. The peak at δ 60.04 is assigned to carbon of carbonitrile, peak at δ 195.81 is assigned to carbonyl carbon and peaks at δ 105.21-160.68 are attributed to aromatic carbons.

Additionally, all the reactions have also been performed under classical heating conditions. The comparison of the results for the 20 compounds listed in **Table I** indicates that the reactions are efficiently promoted by microwave irradiation. The reaction time was strikingly shortened from 2-2.5 hr (in traditional heating condition) to 2-4 min (under microwave irradiation) and quantitative yields were obtained.

## Antimicrobial activity

All the newly synthesized compounds **4a-t** were screened for their antibacterial activity *in vitro* against Gram-negative bacterium *Escherichia coli* and Gram-positive bacterium *Bacillus subtilis, Staphylococcus aureus* using Ampicillin and Ciprofloxacin as a standard and antifungal activity against *Rhizopus* and *Aspergillius niger* using Griseofulvin as a standard. The disc diffusion method[22] was used and nutrient agar and potato dextrose agar were used to culture the bacteria and fungus respectively. The compounds were dissolved in DMF and tested against microorganism species at 1000 ppm concentration. The plates were incubated for 24 hr at 35°C for the bacteria and for 48 hr at 28°C for fungus to record the diameter of inhibition zone. The results are summarized in **Table II**.

## Experimental Section

Melting points were recorded by open capillary method and are uncorrected. The IR spectra were recorded on Shimadzu FT-IR-S8401 spectrometer in KBr. $^1$H and $^{13}$C NMR spectra were recorded on a Bruker Avance 400 MHz spectrometer using solvent

**Table I** — Comparison of microwave and conventional method and physical data of the compounds **4a-t**

| Compd | R | R′ | Microwave | | Conventional | | m.p.[b] (°C) |
|---|---|---|---|---|---|---|---|
| | | | Time (min) | Yield[a] (%) | Time (hr) | Yield[a] (%) | |
| **4a** | H | H | 2.5 | 89 | 2 | 75 | 245-48(d) |
| **4b** | $CH_3$ | H | 3 | 82 | 2 | 73 | 264-66(d) |
| **4c** | $OCH_3$ | H | 2.5 | 85 | 2 | 70 | 271-73 |
| **4d** | Cl | H | 4[c] | 75 | 2.5 | 60 | 255-57 |
| **4e** | H | $CH_3$ | 2.5 | 80 | 2 | 69 | 247-49(d) |
| **4f** | $CH_3$ | $CH_3$ | 2.5 | 82 | 2 | 73 | 243-45(d) |
| **4g** | $OCH_3$ | $CH_3$ | 2 | 83 | 2 | 68 | 248-50 |
| **4h** | Cl | $CH_3$ | 3.5[c] | 72 | 2.5 | 59 | 269-70 |
| **4i** | H | $OCH_3$ | 3 | 84 | 2 | 71 | 250-53(d) |
| **4j** | $CH_3$ | $OCH_3$ | 2.5 | 87 | 2 | 73 | 249-51(d) |
| **4k** | $OCH_3$ | $OCH_3$ | 3 | 79 | 2 | 68 | 238-40 |
| **4l** | Cl | $OCH_3$ | 4[c] | 73 | 2.5 | 58 | 279-81(d) |
| **4m** | H | Cl | 2.5 | 85 | 2 | 70 | 258-60(d) |
| **4n** | $CH_3$ | Cl | 3 | 83 | 2 | 72 | 260-63(d) |
| **4o** | $OCH_3$ | Cl | 3 | 87 | 2 | 70 | 262-64(d) |
| **4p** | Cl | Cl | 4[c] | 70 | 2.5 | 55 | 274-75 |
| **4q** | H | $COCH_3$ | 3.5 | 85 | 2.5 | 72 | 225-27 |
| **4r** | $CH_3$ | $COCH_3$ | 3 | 88 | 2.5 | 73 | 218-20 |
| **4s** | $OCH_3$ | $COCH_3$ | 3.5 | 82 | 2.5 | 70 | 250-52(d) |
| **4t** | Cl | $COCH_3$ | 4.5[c] | 70 | 2.5 | 57 | 268-70(d) |

[a] Yield corresponds to crude product (d) Decomposes
[b] After crystallization [c] Irradiated at 350 W

peak as internal standard. Elemental analyses were carried out using Perkin-Elmer 2400 series II analyzer. The microwave oven used was specially modified by RAGA's electromagnetic systems.

### General procedure for the synthesis of [(2-chloro-6-(un)substituted-3-quinolyl) methylene]methane-1,1-dicarbonitrile compounds, 2a-d

2-Chloro-3-formyl quinolines **1a-d** (0.01 mole), malononitrile (0.01 mole) and ethanol (2-3 mL) were charged in round bottom flask and contents in the flask were mixed thoroughly so as to obtain a paste. Then 1-2 drop of piperidene was added. The flask was heated under microwave irradiation at 240 W for 1 to 1.5 min. After the completion of reaction (checked by TLC, ethylacetate:hexane, 10:90), the product **2a-d** was filtered and washed with ethanol. The product was purified by recrystallization from ethyl acetate.

### [(2-Chloro-3-quinolyl)methylene]methane-1,1-dicarbonitrile, 2a

IR (KBr): 3040 (aromatic C-H str.), 2240 (CN str.), 1570, 1480 (C=C str. of aromatic ring), 745 $cm^{-1}$ (C-Cl str.); $^1H$ NMR (400 MHz, $CDCl_3$) : δ 7.18-8.93(1H, s, -CH=C- and 5H, m, Ar-H); $^{13}C$ NMR (400 MHz, $CDCl_3$): δ 88.45, 105.35, 111.48, 113.80, 123.32, 127.59, 128.56, 130.55, 137.38, 144.12, 145.24, 155.11, 159.07. Anal. Calcd. for $C_{13}H_6N_3Cl$: C, 65.14; H, 2.52; N, 17.5. Found: C, 65.22; H, 2.68; N, 17.35%.

### General procedure for the synthesis 2-amino-4-(2-chloro-6-(un)substituted-(3-quinolyl))-7,7-dimethyl-5-oxo-1-aryl-1,4,6,7,8-pentahydro quinoline -3-carbonitrile compounds, 4a-t

### Conventional synthesis

[(2-Chloro-3-quinolyl)methylene]methane-1,1-dicarbonitriles **2a-d** (0.001 mole), 3-arylamino-5,5-dimethyl-cyclohex-2-en-1-ones **3a-e** (0.001 mole), DMAP (15 mole %) and absolute ethanol (5 mL) were charged in round bottom flask. Then the reaction mixture was refluxed for 2-2.5 hr. The completion of the reaction was monitored by the TLC (Ethyl acetate: Hexane, 4:6). The solid product **4a-t** separated was filtered off and purified using chloroform-methanol.

**Table II** — Antimicrobial activity of compounds **4a-t**

| Compd | Antibacterial activity Inhibition zone in mm | | | Antifungal activity Inhibition zone in mm | |
|---|---|---|---|---|---|
| | *E. coli* | *B. substilis* | *S. aureus* | *Rhizopus* | *A. niger* |
| **4a** | 23 | 17 | 14 | 14 | 12 |
| **4b** | 22 | 22 | 14 | 15 | 13 |
| **4c** | 24 | 17 | 13 | 14 | 10 |
| **4d** | 23 | 18 | 20 | 18 | 11 |
| **4e** | 24 | 14 | 19 | 19 | 17 |
| **4f** | 23 | 09 | 12 | 18 | 15 |
| **4g** | 23 | 11 | 16 | 16 | 10 |
| **4h** | 27 | 17 | 13 | 16 | 14 |
| **4i** | 24 | 14 | 16 | 19 | 16 |
| **4j** | 26 | 18 | 17 | 23 | 20 |
| **4k** | 23 | 17 | 16 | 20 | 17 |
| **4l** | 20 | 14 | 13 | 18 | 15 |
| **4m** | 16 | 15 | 16 | 15 | 17 |
| **4n** | 19 | 19 | 14 | 17 | 16 |
| **4o** | 21 | 18 | 15 | 18 | 11 |
| **4p** | 20 | 20 | 16 | 17 | 13 |
| **4q** | 22 | 16 | 13 | 16 | 17 |
| **4r** | 25 | 15 | 16 | 12 | 16 |
| **4s** | 21 | 15 | 14 | 17 | 18 |
| **4t** | 24 | 14 | 14 | 12 | 17 |
| Ampicillin | 31 | 33 | 33 | -- | -- |
| Ciprofloxacin | 35 | 37 | 34 | -- | -- |
| Griseofulvin | -- | -- | -- | 28 | 21 |

## Microwave-induced synthesis

[(2-Chloro-3-quinolyl)methylene]methane-1,1-di-carbonitriles **2a-d** (0.001 mole), 3-arylamino-5,5-dimethyl-cyclohex-2-en-1-ones **3a-e** (0.001 mole), DMAP (15 mole %) and absolute ethanol (0.5 mL) were charged in round bottom flask and contents in the flask were mixed thoroughly so as to obtain a paste. The flask was heated under microwave irradiation at 240 W for 2-4.5 min. After the completion of reaction (checked by TLC, ethylacetate:hexane, 40:60), the solid product **4a-t** was filtered and washed with ethanol. The product was purified using chloroform-methanol.

### 2-Amino-4-(2-chloro(3-quinolyl))-7,7-dimethyl-5-oxo-1-phenyl-1,4,6,7,8-pentahydro quinoline -3-carbonitrile, 4a

IR (KBr): 3440 (asym.N-H str.), 3350 (sym.N-H str.), 3000 (aromatic C-H str.), 2170 (-CN str.), 1690 $cm^{-1}$ ( C=O str.); $^1$H NMR (400 MHz, $CDCl_3$) : δ 0.93 (s, 3H, $CH_3$), 0.97 (s, 3H, $CH_3$), 1.72-2.22 (m, 4H, 2 × $CH_2$), 4.17 (s, 2H, $NH_2$), 5.24 (s, 1H, CH), 7.28-8.25 (m, 10H, Ar-H); $^{13}$C NMR (400 MHz, $CDCl_3$): δ 27.25, 29.39, 32.27, 37.56, 41.88, 49.79, 60.41, 109.78, 120.58, 126.96, 127.45, 127.81,127.96, 130.12, 130.57, 130.74, 131.34, 134.42, 135.79, 140.14, 146.70, 149.71, 151.20, 151.26, 195.78; Anal. Calcd. for $C_{27}H_{23}ClN_4O$: C, 71.28; H, 5.096; N, 12.31. Found: C, 71.43; H, 5.12; N,12.10%.

### 2-Amino-4-(2-chloro-6-methyl(3-quinolyl))-7,7-dimethyl-5-oxo-1-phenyl-1,4,6,7,8-pentahydro quinoline -3-carbonitrile, 4b

IR (KBr): 3450 (asym.N-H str.), 3320 (sym.N-H str.), 3010 (aromaticC-H str.), 2880 (aromatic methyl C-H str.), 2190 (-CN str.), 1690 $cm^{-1}$ (C=O str.); $^1$H NMR (400 MHz, $CDCl_3$): δ 0.93 (s, 3H, $CH_3$), 0.97 (s, 3H, $CH_3$), 1.70-2.21 (m, 4H, 2 × $CH_2$), 2.49 (s, 3H, $CH_3$), 4.14 (s, 2H, $NH_2$), 5.22 (s, 1H, CH), 7.22-8.12 (m, 9H, Ar-H); $^{13}$C NMR (400 MHz, $CDCl_3$): δ 21.30, 27.22, 29.41, 32.24, 37.43, 41.81, 49.70, 60.35, 109.80, 120.69, 126.72, 127.48, 127.74,128.44, 129.92, 130.55, 131.10,

134.1, 136.00, 139.94, 142.64,146.12, 150.10, 152.0, 152.30, 195.72. Anal. Calcd. for $C_{28}H_{25}ClN_4O$: C, 71.71; H, 5.73; N, 11.94. Found: C, 71.53; H, 5.65; N, 12.01%.

**2-Amino-4-(2-chloro-6-methyl(3-quinolyl))-7,7-dimethyl-1-(4-methylphenyl)-5-oxo 1,4,6,7,8-pentahydro quinoline -3-carbonitrile, 4f**

IR (KBr): 3500 (asym. N-H str.), 3360 (sym. N-H str.), 2980 (aromatic C-H str.), 2870 (aromatic methyl C-H str.), 2180 (-CN str.), 1690 $cm^{-1}$ (C=O str.); $^1H$ NMR (400 MHz, $CDCl_3$): δ 0.93 (s, 3H, $CH_3$), 0.97 (s, 3H, $CH_3$), 1.89-2.20 (m, 4H, 2 × $CH_2$),2.50 (s, 3H, $CH_3$), 2.54 (s, 3H, $CH_3$) 4.13 (s, 2H, $NH_2$), 5.21 (s, 1H, CH), 7.21-8.15 (m, 8H, Ar-H); $^{13}C$ NMR (400 MHz, $CDCl_3$): δ 21.34, 21.63, 27.27, 29.42, 32.25, 37.33, 41.83, 49.79, 60.30, 109.82, 120.73, 126.59, 127.50, 127.60, 129.72, 131.16, 132.34, 133.00, 134.55, 136.86, 139.39, 140.90, 145.28, 148.85, 151.32, 151.45, 195.74. Anal. Calcd. for $C_{29}H_{27}ClN_4O$: C, 72.11; H, 5.63; N, 11.59. Found: C, 72.20; H, 5.56; N, 11.67%.

**2-Amino-4-(2-chloro-6-methoxy(3-quinolyl))-7,7-dimethyl-1-(4-methylphenyl)-5-oxo 1,4,6,7,8-pentahydro quinoline -3-carbonitrile, 4g**

IR (KBr): 3460 (asym.N-H str.), 3360 (sym.N-H str.), 3040 (aromatic C-H str.), 2960 (aromatic methoxy C-H str.), 2880 (aromatic methyl C-H str.), 2170 (-CN str.), 1690 $cm^{-1}$ (C=O str.); $^1H$ NMR (400 MHz, $CDCl_3$): δ 0.94 (s, 3H, $CH_3$), 0.97 (s, 3H, $CH_3$), 1.88-2.24 (m, 4H, 2 × $CH_2$), 2.49 (s, 3H, $CH_3$), 3.94 (s, 3H, $OCH_3$), 4.14 (s, 2H, $NH_2$), 5.18 (s, 1H, CH), 7.12-8.16 (m, 8H, Ar-H); $^{13}C$ NMR (400 MHz, $CDCl_3$): δ 21.31, 27.30, 29.36, 32.22, 37.82, 41.84, 49.83, 55.62, 60.11, 105.21, 109.53, 120.73, 122.85, 128.49, 129.31, 131.64, 132.56, 133.02, 134.40, 139.15, 140.88, 142.74, 147.17, 151.40, 151.53, 158.05, 195.77. Anal. Calcd. for $C_{29}H_{27}ClN_4O_2$: C, 69.80; H, 5.45; N, 11.22. Found: C, 69.62; H, 5.56; N, 11.12%.

**2-Amino-4-(2-chloro-6-methoxy(3-quinolyl))-1-(4-methoxyphenyl)-7,7-dimethyl-5-oxo-1,4,6,7,8-pentahydro quinoline-3-carbonitrile, 4k**

IR (KBr): 3470 (asym. N-H str.), 3350 (sym. N-H str.), 3040 (aromatic C-H str.), 2850 (aromatic methoxy C-H str.), 2210 (-CN str.), 1650 $cm^{-1}$ (C=O str.); $^1H$ NMR (400 MHz, $CDCl_3$): δ 0.93 (s, 3H, $CH_3$), 0.97 (s, 3H, $CH_3$), 1.69-2.20 (m, 4H, 2 × $CH_2$), 3.91 (s, 3H, $OCH_3$), 3.94 (s, 3H, $OCH_3$), 4.18 (s, 2H, $NH_2$), 5.17 (s, 1H, CH), 7.08-8.15 (m, 8H, Ar-H); $^{13}C$ NMR (400 MHz, $CDCl_3$): δ 27.32, 29.41, 32.19, 37.93, 41.87, 49.80, 55.63, 55.73,60.04, 105.21, 109.48, 115.80, 120.74, 122.90, 127.92, 128.47, 129.30, 131.32,134.20, 139.21, 142.75, 147.11, 151.60, 151.82, 158.06, 160.68, 195.81. Anal. Calcd. for $C_{29}H_{27}ClN_4O_3$: C, 67.63; H, 5.28; N, 10.87. Found: C, 67.52; H, 5.36; N, 10.98%.

**2-Amino-4-(2,6-dichloro(3-quinolyl))-1-(4-methoxyphenyl)-7,7-dimethyl-5-oxo-1,4,6,7,8-pentahydro quinoline-3-carbonitrile, 4l**

IR (KBr): 3480 (asym. N-H str.), 3360 (sym. N-H str.), 3000 (aromatic C-H str.), 2965 (aromatic methoxy C-H str.), 2190 (-CN str.), 1700 (C=O str.), 790 $cm^{-1}$ (C-Cl str.); $^1H$ NMR (400 MHz, $CDCl_3$): δ 0.93 (s, 3H, $CH_3$), 0.97 (s, 3H, $CH_3$), 1.88-2.21 (m, 4H, 2 × $CH_2$), 3.90 (s, 3H, $OCH_3$), 4.14 (s, 2H, $NH_2$), 5.12 (s, 1H, CH), 7.15-8.20 (m, 8H, Ar-H); $^{13}C$ NMR (400 MHz, $CDCl_3$): δ 27.10, 29.60, 32.54, 39.08, 42.10, 50.06, 55.60, 60.04, 105.42, 109.58, 115.60, 121.04, 123.10, 128.24, 128.60, 129.50, 130.80, 131.72, 134.52, 140.12, 142.90, 147.41, 151.94, 158.24, 160.78, 195.81. Anal. Calcd. for $C_{28}H_{24}Cl_2N_4O_2$: C, 64.74; H, 4.65; N, 10.78. Found: C, 64.62; H, 4.76; N, 10.84%.

**2-Amino-4-(2-chloro-6-methyl (3-quinolyl))-1-(4-chlorophenyl)-7, 7-dimethyl-5-oxo-1,4,6,7,8-pentahydro quinoline-3-carbonitrile, 4n**

IR (KBr): 3490 (asym. N-H str.), 3340 (sym. N-H str.), 2980 (aromatic C-H str.), 2875 (aromatic methyl C-H str.), 2200 (-CN str.), 1690 $cm^{-1}$ ( C=O str.); $^1H$ NMR (400 MHz, $CDCl_3$) : δ 0.93 (s, 3H, $CH_3$), 0.97 (s, 3H, $CH_3$), 1.84-2.24 (m, 4H, 2 × $CH_2$), 2.56 (s, 3H, $CH_3$), 4.16 (s, 2H, $NH_2$), 5.218 (s, 1H, CH), 7.16-8.16 (m, 8H, Ar-H); $^{13}C$ NMR (400 MHz, $CDCl_3$): δ 21.65, 27.3, 29.38, 32.52, 37.44, 41.98, 50.12, 60.54, 109.00, 120.84, 126.88, 127.68, 128.04, 129.94, 131.32, 132.72, 133.36, 134.56, 136.94, 139.55, 141.10, 145.34, 148.92, 151.42, 151.65, 195.76. Anal. Calcd. for $C_{28}H_{24}Cl_2N_4O$: C, 66.08; H, 4.80; N, 11.12. Found: C, 66.17; H, 4.68; N, 11.21%.

**2-Amino-4-(2,6-dichloro(3-quinolyl))-1-(4-chlorophenyl)-7,7-dimethyl-5-oxo-1,4,6,7,8-pentahydro quinoline-3-carbonitrile, 4p**

IR (KBr): 3460 (asym. N-H str.), 3340 (sym. N-H str.), 2990 (aromatic C-H str.), 2210 (-CN str.), 1690 ( C=O str.), 780 $cm^{-1}$ (C-Cl str.); $^1H$ NMR (400 MHz,

$CDCl_3$): δ 0.93 (s, 3H, $CH_3$), 0.97 (s, 3H, $CH_3$), 1.86-2.24 (m, 4H, 2 × $CH_2$), 4.14 (s, 2H, $NH_2$), 5.22 (s, 1H, CH), 7.28-8.25 (m, 8H, Ar-H); $^{13}$C NMR (400 MHz, $CDCl_3$): δ 27.27, 29.44, 32.52, 37.62, 41.94, 49.85, 60.66, 109.87, 120.64, 121.56, 126.92, 127.55, 127.94,128.04, 130.22, 130.67, 130.96, 134.54, 135.87, 140.26, 146.78, 149.84, 151.20, 151.28, 195.72. Anal. Calcd. for $C_{27}H_{21}Cl_3N_4O$: C, 61.90; H, 4.04; N, 10.69. Found: C, 61.94; H, 4.13; N, 10.72%.

**2-Amino-4-(2-chloro(3-quinolyl))-1-(4-acetylphenyl) -7,7-dimethyl-5-oxo-1,4,6,7,8-pentahydroquinoline-3-carbonitrile, 4q**

IR (KBr): 3440 (asym. N-H str.), 3370 (sym. N-H str.), 3010 (aromatic C-H str.), 2210 (-CN str.), 1700 cm$^{-1}$ (C=O str.); $^1$H NMR (400 MHz, $CDCl_3$): δ 0.94 (s, 3H, $CH_3$), 0.97 (s, 3H, $CH_3$), 1.85-2.22 (m, 4H, 2 × $CH_2$), 2.76 (s, 3H, $COCH_3$), 4.10 (s, 2H, $NH_2$), 5.23 (s, 1H, CH), 7.28-8.27 (m, 9H, Ar-H); $^{13}$C NMR (400 MHz, $CDCl_3$): δ 27.20, 27.38, 29.36, 32.68, 37.44, 42.0, 49.64, 60.52,109.12, 120.64, 121.46, 126.84, 127.42, 127.88, 128.12, 130.42, 130.83, 130.84, 132.64, 134.68, 135.96, 140.12, 146.84, 149.195, 151.20, 194.20, 195.72. Anal. Calcd. for $C_{29}H_{25}ClN_4O_2$: C, 70.0; H, 5.07; N, 11.27. Found: C, 70.11; H, 5.15; N, 11.19%.

## Conclusion

Simple, efficient and environmentally benign method has been developed for the synthesis of new biquinoline derivatives under microwave irradiation conditions in presence of catalytic amount of DMAP. This microwave irradiation method is superior from the view of yield and reaction time compared to the conventional method.

Screening results revealed that most of the compounds are having significant activity against Gram-positive bacterium, Gram-negative bacterium and fungi. Among all compounds **4h**, **4j**, **4r** against *E. coli,* **4b**, **4n**, **4p** against *B. substilis* and **4d**, **4e, 4j** against *S. aureus* showed promising activity. Compounds **4e**, **4i**, **4j**, **4k** and **4j**, **4s** showed promising activity aginst *Rhizopus* and *A. niger* respectively. Compounds **4f**, **4g** and **4c**, **4f**, **4h** exhibited weak activity against *B. substilis* and *S. aureus* respectively while compounds **4r**, **4t** and **4a**, **4b**, **4p** showed weak activity against *Rhizopus* and *A. niger* respectively.

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## References

1 (a) Kappe C O & Stadler A, *Microwaves in Organic and Medicinal Chemistry*, (Wiley-VCH, Weinheim), **2005**; (b) Al-Obeidi F, Austin R E, Okonya J F & Bond D R S, *Mini-Rev Med Chem*, 3, **2003**, 449.

2 (a) Dabiri M, Delbari A S & Benzir A, *Synlett*, **2007**, 0281; (b) Xia M & Lu Y D, *J Mol Catal A*, 265, **2006**, 206.

3 Desai A R & Desai K R, *Arkivoc*,(xiii), **2005**, 98.

4 (a) Rao H S & Senthilkumar S P, *Indian J Chem*, 43B, **2004**, 2426; (b) Nandagopal S, Annie G & Perumal P T, *Indian J Chem*, 42B, **2003**, 2426.

5 Berry D J, Digiovanna C V, Metrick S S & Murugan R, *Arkivoc*, (i), **2001**, 201.

6 Craig J C & Person P E, *J Med Chem,* 14, **1971**, 1221.

7 Dillard R D, Pravey D E & Benslay D N, *J Med Chem,* 16, **1973**, 251.

8 Patel H V, Vyas K V & Fernandes P S, *Indian J Chem,* 29B, **1990**, 836.

9 Moiseev I K, Zemtsova M N, Trakhtenberg P L, Kulikowa D A, Pskobkina I, Neshchadim G N & Ostapchuk N V, *Khim Farm Zh*, 22, **1998**, 1448.

10 D Wu, *Tetrahedron*, 59, **2003**, 8649.

11 Campbell N, *Rodd's Chemistry of Carbon Compounds,* edited by E H Rodd (Elsevier Scientific Publishing Company, Amsterdam), Vol. IVF, **1976**, 231.

12 Ali B F, Al-Sou'od K, Al-Ja'ar N, Nassar A, Zaghal M H, Judeh Z, Al-Far R, Al-Refai M, Ibrahim M, Mansi K & Al-Obaidi K H, *J Coord Chem*, 59, **2006**, 229.

13 Gao E-J, Zhao S-M, Liu Q-T & Xu R, *Acta Chimica Sinica*, 62, **2004**, 593.

14 Fukuuchi T, Doh-ura K, Yoshihara S & Ohta S, *Bioorg Med Chem Lett*, 16, **2006**, 5982.

15 (a) Lyakhovnenko A S, Trifonov V V, Goncharov V I & Aksenov A V, *Chem Heterocycl Comp*, 42, **2006**, 1205; (b) Trifonov V V, Goncharov V I & Aksenov A V, *Chem Heterocycl Comp*, 42, **2006**, 955; (c) Antonova O A, Goncharov V I & Aksenov A V, *Chem Heterocycl Comp*, 42, **2006**, 197; (d) Trifonov V V, Aksenova I V, Goncharov V I & Aksenov A V, *Chem Heterocycl Comp*, 42, **2006**, 1541.

16 (a) Kobayashi K, Yonemori J, Matsunaga A, Kitamura T, Miyuki T, Morikawa O & Konishi H, *Heterocycles*, **2001**, 33; (b) Ichikawa J, Mori T, Miyazaki H & Wada Y, *Synlett*, **2004**, 1219.

17 Gorlitzer K, Weber F & Jones P G, *Pharmazie*, 61, **2006**, 183.

18 Broch S, Anizon F & Moreau P, *Synthesis*, **2008**, 2039.

19 Patel R D, Patel M P & Patel R G, *Indian J Chem*, 44B, **2005**, 1944.

20 Meth-Cohn O, Narine B & Tarnowski B, *J Chem Soc Perkin Trans 1,* **1981**, 1520.

21 Chanda K, Dutta M C & Vishwakarma J N, *Indian J Chem*, 43B, **2004**, 2475.

22 Colle J G, Duguid J P, Fraser A G & Marmion B P, *Mackie and Mc Cartney Practical Medical Microbiology*, Vol 2, 13th edn (Churchil Livingstone, London) **1989**.