

## A Clean Synthesis of 1,4-Diarylquinoline Derivatives Catalyzed by TEBAC in Aqueous Media

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A series of 1,4-diarylquinoline derivatives were synthesized by the reaction of arylmethylidene-malononitriles or 2-cyano-3-aryl-1-acrylate and 3-arylamino-5,5-dimethylcyclohex-2-enone in aqueous media at 100 °C catalyzed by TEBAC. Meanwhile, the water medium was chosen as green solvent.

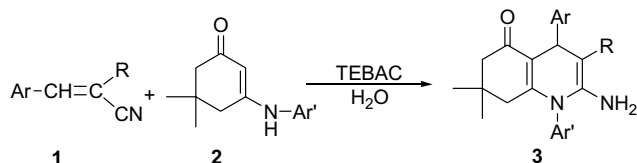
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Most chemical reactions of organic substances conducted in the laboratory as well as in industry need organic solvents as reaction media, although water is safe, benign, environmentally friendly and cheap compared with organic solvents. In the 1980s, Breslow discovered that a Diels-Alder reaction performed in water can be subject to huge accelerations.<sup>1</sup> The observation led to increased interest from synthetic organic chemists to organic reactions in water. In the past ten years, water used as medium has been reported for a large number of organic reactions, such as Claisen rearrangement,<sup>2</sup> Diels-Alder reactions,<sup>3</sup> Reformatsky reactions<sup>4</sup> and many other reactions.<sup>5</sup>

Quinoline derivatives are a class of important compounds, which are widely ascribed to have antitumor,<sup>6</sup> antibacterial,<sup>7</sup> anti-plasmodial,<sup>8</sup> antimalarial<sup>9</sup> and anticancer activities.<sup>10</sup> The traditional methods available for the synthesis of quinolines are either in organic solvents or ordinary 4-arylquinolines.<sup>11</sup> Because of the toxic and volatile nature of many organic solvents, we investigated the synthesis of these potential active compounds mentioned above under environmentally friendly conditions. Particularly, we focused our attention on the use of water as reaction medium. Here we would like to report the synthesis of 1,4-diarylquinoline derivatives by the reaction of arylmethylidene-malononitriles or 2-cyano-3-aryl-1-acrylate and 3-arylamino-5,5-dimethylcyclohex-2-enone in aqueous media at 100 °C catalyzed by TEBAC.

We began our study of the reaction shown in Scheme I by optimizing the reaction conditions for the preparation of

**Scheme I**



1,4-diarylquinolines **3a**. A summary of the optimization experiment is provided in Table 1. It turned out that at room temperature, no reaction took place even when the amount of catalyst (TEBAC) was increased to 20 mol% (Table 1, entries 1 and 2). The catalyst plays a crucial role in the success of the reaction in terms of the rate and the yields. From Table 1, we can see using just 10 mol% TEBAC at reflux in water is sufficient to make the reaction happen. More catalyst does not result in a greater improvement of this reaction. To find the optimum reaction time, the reaction was carried out in the presence of a certain amount of TEBAC (here we used 10 mol%) for 8, 10, or 12 hours, leading to **3a** in 72%, 93% and 93% yield, respectively. Thus, the optimal reaction times and catalyst amount is 10 hours and 10 mol% TEBAC, respectively. In addition, CH<sub>3</sub>(CH<sub>2</sub>)<sub>15</sub>NMe<sub>3</sub>Br and CH<sub>3</sub>(CH<sub>2</sub>)<sub>11</sub>SO<sub>3</sub>Na were also tested as catalysts. In these cases, product **3a** was formed in slightly lower yields (Table 1, entries 9-10). Moreover the catalyst of TEBAC together with water can be reused for the synthesis of **3a** without significant loss of activity; perhaps the product in the reused TEBAC and water has saturated, which made the yield slightly higher in the second and third runs. The

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Table 1. Synthesis of **3a** in water under different reaction conditions<sup>a</sup>

Entry	Temperature/°C	Amount/mol%	Catalyst	Time/h	Yield <sup>b</sup> /(%)
1	r.t.	10	TEBAC	10	0
2	r.t.	20	TEBAC	10	0
3	50	10	TEBAC	10	52
4	100	10	TEBAC	8	72
<b>5</b>	<b>100</b>	<b>10</b>	<b>TEBAC</b>	<b>10</b>	<b>93</b>
6	100	10	TEBAC	12	93
7	100	5	TEBAC	10	83
8	100	20	TEBAC	10	92
9	100	10	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>15</sub> NMe <sub>3</sub> Br	10	91
10	100	10	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>11</sub> SO <sub>3</sub> Na	10	89

<sup>a</sup> Reaction condition: 10 mL water, 2 mmol **1a** and 2 mmol **2a**.<sup>b</sup> Isolated yields.Table 2. Reuse of the catalyst for synthesis of **3a**<sup>a</sup>

Round	1	2	3	4
Yield <sup>b</sup>	93	94	94	92

<sup>a</sup> Reaction condition: 10 mL water, 2 mmol **1a** and 2 mmol **2a**.<sup>b</sup> Isolated yields.

results are summarized in Table 2.

In order to apply this reaction to a library synthesis, various kinds of 3-arylamino-5,5-dimethylcyclohex-2-enone **1** and arylmethylidenemalononitriles or 2-cyano-3-aryl-1-acrylate **2** were subjected to give the corresponding 1,4-diarylquinolines **3**, and representative examples are shown

in Table 3. All of **1** and **2** gave expected products in high yields, either bearing electron-withdrawing groups (such as halide, nitro) or electron-donating groups (such as alkyl group, alkoxy group) under the same reaction conditions. So we concluded that no obvious effects from the electronic or nature of the aromatic ring substituents were observed in the above reactions.

Products **3** were completely characterized by IR, <sup>1</sup>H NMR and elemental analyses. The analyses were in agreement with their structures. The melting points of the known compounds were in accordance with those in the literature. In order to further confirm the structure, the X-ray diffraction analysis<sup>12</sup> of the product **3g** was carried out. As ex-

Table 3. The reaction times and yields of the products **3**

Entry	Ar	Ar'	R	Time (h)	Yields (%)
<b>3a</b>	4-ClC <sub>6</sub> H <sub>4</sub>	C <sub>6</sub> H <sub>5</sub>	CN	10	93
<b>3b</b>	3-ClC <sub>6</sub> H <sub>4</sub>	4-FC <sub>6</sub> H <sub>4</sub>	CN	14	89
<b>3c</b>	3,4-(CH <sub>3</sub> ) <sub>2</sub> C <sub>6</sub> H <sub>3</sub>	4-ClC <sub>6</sub> H <sub>4</sub>	CN	12	89
<b>3d</b>	2,4-Cl <sub>2</sub> C <sub>6</sub> H <sub>3</sub>	4-BrC <sub>6</sub> H <sub>4</sub>	CN	10	90
<b>3e</b>	3-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	4-BrC <sub>6</sub> H <sub>4</sub>	CN	10	94
<b>3f</b>	4-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	4-BrC <sub>6</sub> H <sub>4</sub>	CN	14	88
<b>3g</b>	2-ClC <sub>6</sub> H <sub>4</sub>	4-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	CN	8	93
<b>3h</b>	4-FC <sub>6</sub> H <sub>4</sub>	4-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	CN	8	97
<b>3i</b>	3-ClC <sub>6</sub> H <sub>4</sub>	4-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	CN	8	93
<b>3j</b>	4-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub>	4-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	CN	10	90
<b>3k</b>	4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	4-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	CN	8	98
<b>3l</b>	3-ClC <sub>6</sub> H <sub>4</sub>	4-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	CO <sub>2</sub> Et	16	87
<b>3m</b>	2-ClC <sub>6</sub> H <sub>4</sub>	4-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	CO <sub>2</sub> Et	16	79
<b>3n</b>	4-ClC <sub>6</sub> H <sub>4</sub>	4-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	CO <sub>2</sub> Et	17	81
<b>3o</b>	2,4-Cl <sub>2</sub> C <sub>6</sub> H <sub>3</sub>	4-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	CO <sub>2</sub> Et	16	82
<b>3p</b>	3-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	4-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	CO <sub>2</sub> Et	18	83
<b>3q</b>	3-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	4-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	CO <sub>2</sub> Me	17	80
<b>3r</b>	4-ClC <sub>6</sub> H <sub>4</sub>	C <sub>6</sub> H <sub>5</sub>	CO <sub>2</sub> Et	20	81
<b>3s</b>	3-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	4-FC <sub>6</sub> H <sub>4</sub>	CO <sub>2</sub> Et	18	81

pected, the structure we obtained was 2-amino-7,7-dimethyl-4-(2-chlorophenyl)-1-(4-methylphenyl)-5-oxo-1,4,5,6,7,8-hexahydroquinolin-3-carbonitrile, which is shown in Fig. 1.

## EXPERIMENTAL

Melting points were determined in open capillaries and are uncorrected. IR spectra were recorded on a TENSOR 27 spectrometer in KBr.  $^1\text{H}$  NMR spectra were obtained from solution in  $\text{DMSO-}d_6$  with  $\text{Me}_4\text{Si}$  as internal standard using an Inova-400 spectrometer. Elemental analyses were carried out using a Perkin-Elmer 240 analyzer.

### Typical experimental procedure

A 50 mL flask was charged with arylmethylidene-malononitriles or 2-cyano-3-aryl-1-acrylate **1** (2 mmol), 3-arylamino-5,5-dimethylcyclohex-2-enone **2** (2 mmol), TEBAC (0.2 mmol) and water (10 mL). The mixture was stirred at refluxing temperature for 8~20 h, and then cooled to room temperature. The generated solid was filtered off and washed with water. The crude product was purified by recrystallization from DMF and water to give **3**.

### 2-Amino-4-(4-chlorophenyl)-7,7-dimethyl-5-oxo-1-phenyl-1,4,5,6,7,8-hexahydroquinolin-3-carbonitrile **3a**

Mp 258-260 °C;  $^1\text{H}$  NMR ( $\text{DMSO-}d_6$ ):  $\delta$  0.80 (s, 3H,

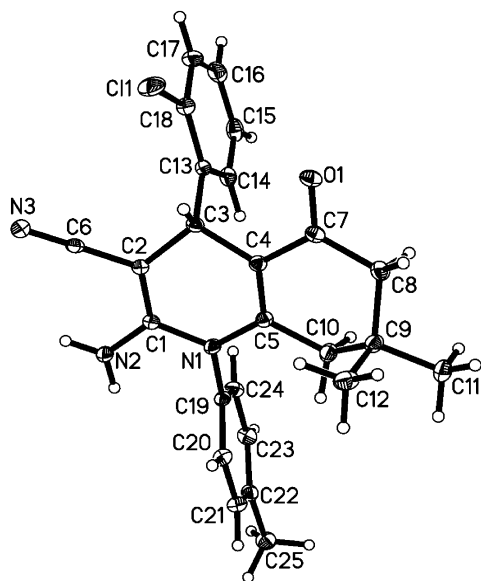


Fig. 1. The crystal structure of compound **3g**.

$\text{CH}_3$ ), 0.89 (s, 3H,  $\text{CH}_3$ ), 1.76 (d,  $J = 17.2$  Hz, 1H, CH), 1.96 (d,  $J = 16.0$  Hz, 1H, CH), 2.18 (d,  $J = 16.0$  Hz, 1H, CH), 2.20 (d,  $J = 17.2$  Hz, 1H, CH), 5.02 (s, 1H, CH), 5.28 (s, 2H,  $\text{NH}_2$ ), 7.19-7.23 (m, 1H, ArH), 7.32-7.39 (m, 3H, ArH), 7.45 (d,  $J = 7.2$  Hz, 2H, ArH), 7.58-7.63 (m, 3H, ArH);  $^{13}\text{C}$  NMR ( $\text{DMSO-}d_6$ ): 26.7, 29.3, 32.1, 33.9, 41.3, 49.4, 110.9, 121.2, 127.8, 128.0, 129.5, 129.9, 130.1, 130.2, 130.4, 131.7, 136.2, 144.0, 151.3, 151.4, 194.8; IR (KBr),  $\nu$ : 3470, 3340, 3063, 2956, 2898, 2867, 2178, 1651, 1619, 1592, 1567, 1488, 1469, 1446, 1415, 1374, 1297, 1261, 1145, 1034, 826, 747, 703.

Anal. Calcd for  $\text{C}_{24}\text{H}_{22}\text{ClN}_3\text{O}$ : C 71.37, H 5.49, N 10.40; found C 71.38, H 5.58, N 10.52.

### 2-Amino-4-(3-chlorophenyl)-1-7,7-dimethyl-(4-fluorophenyl)-5-oxo-1,4,5,6,7,8-hexahydroquinolin-3-carbonitrile **3b**

Mp 276-278 °C;  $^1\text{H}$  NMR ( $\text{DMSO-}d_6$ ):  $\delta$  0.75 (s, 3H,  $\text{CH}_3$ ), 0.90 (s, 3H,  $\text{CH}_3$ ), 1.73 (d,  $J = 17.6$  Hz, 1H, CH), 2.02 (d,  $J = 16.0$  Hz, 1H, CH), 2.19 (d,  $J = 16.0$  Hz, 1H, CH), 2.20 (d,  $J = 17.6$  Hz, 1H, CH), 4.47 (s, 1H, CH), 5.57 (s, 2H,  $\text{NH}_2$ ), 7.25-7.28 (m, 3H, ArH), 7.36-7.44 (m, 2H, ArH);  $^{13}\text{C}$  NMR ( $\text{DMSO-}d_6$ ): 26.4, 29.2, 32.1, 36.6, 41.2, 49.4, 111.3, 117.2, 117.4, 121.5, 125.8, 126.5, 126.9, 130.6, 132.41, 132.44, 133.0, 149.1, 150.8, 151.6, 161.3, 163.7, 195.1; IR (KBr),  $\nu$ : 3464, 3331, 3070, 2966, 2873, 2180, 1654, 1620, 1591, 1569, 1507, 1416, 1372, 1306, 1256, 1226, 1179, 1151, 1090, 1046, 879, 851, 786, 711, 698.

Anal. Calcd for  $\text{C}_{24}\text{H}_{21}\text{ClFN}_3\text{O}$ : C 68.32, H 5.02, N 9.96; found C 68.30, H 5.27, N 9.90.

### 2-Amino-1-(4-chlorophenyl)-4-(3,4-dimethylphenyl)-7,7-dimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinolin-3-carbonitrile **3c**

Mp 264-266 °C;  $^1\text{H}$  NMR ( $\text{DMSO-}d_6$ ):  $\delta$  0.75 (s, 3H,  $\text{CH}_3$ ), 0.89 (s, 3H,  $\text{CH}_3$ ), 1.72 (d,  $J = 17.6$  Hz, 1H, CH), 1.98 (d,  $J = 16.0$  Hz, 1H, CH), 2.17-2.24 (m, 8H, 2CH + 2 $\text{CH}_3$ ), 4.35 (s, 1H, CH), 5.42 (s, 2H,  $\text{NH}_2$ ), 6.92 (d,  $J = 7.6$  Hz, 1H, ArH), 6.99 (s, 1H, ArH), 7.07 (d,  $J = 7.6$  Hz, 1H, ArH), 7.39 (d,  $J = 8.4$  Hz, 2H, ArH), 7.64 (d,  $J = 8.4$  Hz, 2H, ArH);  $^{13}\text{C}$  NMR ( $\text{DMSO-}d_6$ ): 19.2, 19.9, 26.3, 29.4, 32.1, 36.1, 41.1, 49.5, 112.2, 121.7, 124.3, 128.2, 129.7, 130.4, 132.1, 134.2, 134.4, 135.4, 135.9, 144.2, 150.0, 151.1, 195.0; IR (KBr),  $\nu$ : 3460, 3332, 2963, 2936, 2871, 2179, 1654, 1590, 1571, 1521, 1490, 1456, 1416, 1371, 1313, 1255, 1151, 1091, 1042, 1013, 851, 813, 813, 770.

Anal. Calcd for  $C_{26}H_{26}ClN_3O$ : C 72.29, H 6.07, N 9.73; found C 72.20, H 6.20, N 9.80.

**2-Amino-1-(4-bromophenyl)-4-(2,4-dichlorophenyl)-7,7-dimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinolin-3-carbonitrile 3d**

Mp 276-278 °C;  $^1H$  NMR (DMSO- $d_6$ ):  $\delta$  0.80 (s, 3H,  $CH_3$ ), 0.90 (s, 3H,  $CH_3$ ), 1.77 (d,  $J = 17.2$  Hz, 1H, CH), 1.95 (d,  $J = 16.0$  Hz, 1H, CH), 2.17 (d,  $J = 16.0$  Hz, 1H, CH), 2.18 (d,  $J = 17.2$  Hz, 1H, CH), 4.97 (s, 1H, CH), 5.52 (s, 2H,  $NH_2$ ), 7.39-7.43 (m, 4H, ArH), 7.52 (s, 1H, ArH), 7.78 (d,  $J = 8.4$  Hz, 2H, ArH); IR (KBr),  $\nu$ : 3474, 3330, 3100, 2957, 2871, 2173, 1644, 1583, 1560, 1487, 1470, 1420, 1314, 1290, 1254, 1206, 1171, 1141, 1099, 1042, 1011, 847, 809, 759, 739.

Anal. Calcd for  $C_{24}H_{20}BrCl_2N_3O$ : C 55.73, H 3.90, N 8.12; found C 55.62, H 4.07, N 8.20.

**2-Amino-1-(4-bromophenyl)-7,7-dimethyl-4-(3-nitrophenyl)-5-oxo-1,4,5,6,7,8-hexahydroquinolin-3-carbonitrile 3e**

Mp 271-274 °C;  $^1H$  NMR (DMSO- $d_6$ ):  $\delta$  0.72 (s, 3H,  $CH_3$ ), 0.89 (s, 3H,  $CH_3$ ), 1.71 (d,  $J = 17.6$  Hz, 1H, CH), 1.99 (d,  $J = 16.0$  Hz, 1H, CH), 2.18 (d,  $J = 16.0$  Hz, 1H, CH), 2.20 (d,  $J = 17.6$  Hz, 1H, CH), 4.45 (s, 1H, CH), 5.54 (s, 2H,  $NH_2$ ), 7.28 (d,  $J = 8.4$  Hz, 2H, ArH), 7.36-7.38 (m, 4H, ArH), 7.77 (d,  $J = 8.4$  Hz, 2H, ArH); IR (KBr),  $\nu$ : 3462, 3326, 3059, 2964, 2953, 2867, 2179, 1653, 1621, 1570, 1487, 1414, 1372, 1312, 1256, 1173, 1147, 1087, 1069, 1042, 1011, 940, 858, 844, 804, 768, 738.

Anal. Calcd for  $C_{24}H_{21}BrN_4O_3$ : C 58.43, H 4.29, N 11.36; found C 58.30, H 4.33, N 11.39.

**2-Amino-1-(4-bromophenyl)-7,7-dimethyl-4-(4-methylphenyl)-5-oxo-1,4,5,6,7,8-hexahydroquinolin-3-carbonitrile 3f**

Mp 258-261 °C;  $^1H$  NMR (DMSO- $d_6$ ):  $\delta$  0.74 (s, 3H,  $CH_3$ ), 0.90 (s, 3H,  $CH_3$ ), 1.71 (d,  $J = 18.0$  Hz, 1H, CH), 1.99 (d,  $J = 16.0$  Hz, 1H, CH), 2.16-2.27 (m, 5H, 2CH +  $CH_3$ ), 4.40 (s, 1H, CH), 5.46 (s, 2H,  $NH_2$ ), 7.12 (d,  $J = 8.4$  Hz, 2H, ArH), 7.15 (d,  $J = 8.4$  Hz, 2H, ArH), 7.34 (d,  $J = 8.4$  Hz, 2H, ArH), 7.77 (d,  $J = 8.4$  Hz, 2H, ArH); IR (KBr),  $\nu$ : 3458, 3329, 3031, 2962, 2951, 2180, 1655, 1621, 1574, 1486, 1414, 1372, 1256, 1179, 1150, 1070, 1043, 1010, 848, 807, 767.

Anal. Calcd for  $C_{25}H_{23}BrN_3O$ : C 64.94, H 5.23, N 9.09; found C 64.81, H 5.40, N 9.15.

**2-Amino-4-(2-chlorophenyl)-7,7-dimethyl-1-(4-methylphenyl)-5-oxo-1,4,5,6,7,8-hexahydroquinolin-3-carbonitrile 3g**

Mp 254-256 °C;  $^1H$  NMR (DMSO- $d_6$ ):  $\delta$  0.81 (s, 3H,  $CH_3$ ), 0.89 (s, 3H,  $CH_3$ ), 1.79 (d,  $J = 17.6$  Hz, 1H, CH), 1.96 (d,  $J = 16.0$  Hz, 1H, CH), 2.18 (d,  $J = 16.0$  Hz, 1H, CH), 2.20 (d,  $J = 17.6$  Hz, 1H, CH), 2.42 (s, 3H,  $CH_3$ ), 5.01 (s, 1H, CH), 5.23 (s, 2H,  $NH_2$ ), 7.18-7.22 (m, 1H, ArH), 7.31-7.42 (m, 7H, ArH); IR (KBr),  $\nu$ : 3441, 3306, 3068, 2959, 2928, 2871, 2176, 1651, 1621, 1557, 1510, 1469, 1442, 1408, 1316, 1258, 1243, 1152, 1110, 1034, 1022, 942, 847, 820, 761, 707, 674.

Anal. Calcd for  $C_{25}H_{24}ClN_3O$ : C 71.85, H 5.79, N 10.05; found C 71.90, H 5.83, N 9.90.

**2-Amino-7,7-dimethyl-4-(4-fluorophenyl)-1-(4-methylphenyl)-5-oxo-1,4,5,6,7,8-hexahydroquinolin-3-carbonitrile 3h**

Mp 240-242 °C;  $^1H$  NMR (DMSO- $d_6$ ):  $\delta$  0.72 (s, 3H,  $CH_3$ ), 0.87 (s, 3H,  $CH_3$ ), 1.72 (d,  $J = 17.6$  Hz, 1H, CH), 1.99 (d,  $J = 16.0$  Hz, 1H, CH), 2.19 (d,  $J = 16.0$  Hz, 2H, 2CH), 2.40 (s, 3H,  $CH_3$ ), 4.46 (s, 1H, CH), 5.31 (s, 2H,  $NH_2$ ), 7.14 (t,  $J = 8.8$  Hz, 2H, ArH), 7.27-7.31 (m, 4H, ArH), 7.40 (d,  $J = 8.0$  Hz, 2H, ArH); IR (KBr),  $\nu$ : 3467, 3335, 3062, 3030, 2954, 2904, 2863, 2179, 1653, 1618, 1601, 1570, 1507, 1448, 1414, 1387, 1313, 1258, 1218, 1154, 1044, 856, 811, 786.

Anal. Calcd for  $C_{25}H_{24}FN_3O$ : C 74.79, H 6.03, N 10.47; found C 74.70, H 6.13, N 10.52.

**2-Amino-4-(3-chlorophenyl)-7,7-dimethyl-1-(4-methylphenyl)-5-oxo-1,4,5,6,7,8-hexahydroquinolin-3-carbonitrile 3i**

Mp 233-234 °C;  $^1H$  NMR (DMSO- $d_6$ ):  $\delta$  0.74 (s, 3H,  $CH_3$ ), 0.89 (s, 3H,  $CH_3$ ), 1.75 (d,  $J = 17.6$  Hz, 1H, CH), 2.02 (d,  $J = 16.0$  Hz, 1H, CH), 2.20 (d,  $J = 16.8$  Hz, 2H, 2CH), 2.41 (s, 3H,  $CH_3$ ), 4.48 (s, 1H, CH), 5.40 (s, 2H,  $NH_2$ ), 7.24-7.28 (m, 5H, ArH), 7.34-7.42 (m, 3H, ArH); IR (KBr),  $\nu$ : 3464, 3335, 3035, 2961, 2929, 2871, 2179, 1654, 1619, 1568, 1509, 1470, 1416, 1389, 1372, 1307, 1256, 1174, 1145, 1107, 1045, 877, 782, 710.

Anal. Calcd for  $C_{25}H_{24}ClN_3O$ : C 71.85, H 5.79, N 10.05; found C 71.70, H 5.88, N 10.12.

**2-Amino-7,7-dimethyl-4-(4-methoxyphenyl)-1-(4-methylphenyl)-5-oxo-1,4,5,6,7,8-hexahydroquinolin-3-carbonitrile 3j**

Mp 239-241 °C;  $^1H$  NMR (DMSO- $d_6$ ):  $\delta$  0.73 (s, 3H,

CH<sub>3</sub>), 0.88 (s, 3H, CH<sub>3</sub>), 1.71 (d,  $J = 17.6$  Hz, 1H, CH), 1.99 (d,  $J = 16.0$  Hz, 1H, CH), 2.18 (d,  $J = 16.0$  Hz, 1H, CH), 2.19 (d,  $J = 17.6$  Hz, 1H, CH), 2.41 (s, 3H, CH<sub>3</sub>), 3.73 (s, 3H, CH<sub>3</sub>O), 4.40 (s, 1H, CH), 5.25 (s, 2H, NH<sub>2</sub>), 6.88 (d,  $J = 8.8$  Hz, 1H, ArH), 7.18 (d,  $J = 8.4$  Hz, 2H, ArH), 7.26 (d,  $J = 8.8$  Hz, 2H, ArH), 7.40 (d,  $J = 8.4$  Hz, 2H, ArH); IR (KBr),  $\nu$ : 3468, 3337, 3055, 2957, 2930, 2869, 2838, 2176, 1655, 1620, 1583, 1565, 1559, 1463, 1448, 1410, 1373, 1300, 1257, 1213, 1151, 1030, 844, 813, 796, 741, 670.

Anal. Calcd for C<sub>26</sub>H<sub>27</sub>N<sub>3</sub>O: C 75.52, H 6.58, N 10.16; found C 75.69, H 6.60, N 10.07.

**2-Amino-7,7-dimethyl-1-(4-methylphenyl)-4-(4-nitrophenyl)-5-oxo-1,4,5,6,7,8-hexahydroquinolin-3-carbonitrile 3k**

Mp 260-262 °C; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>):  $\delta$  0.73 (s, 3H, CH<sub>3</sub>), 0.89 (s, 3H, CH<sub>3</sub>), 1.76 (d,  $J = 17.6$  Hz, 1H, CH), 2.00 (d,  $J = 16.0$  Hz, 1H, CH), 2.18-2.23 (m, 2H, 2CH), 2.42 (s, 3H, CH<sub>3</sub>), 4.61 (s, 1H, CH), 5.47 (s, 2H, NH<sub>2</sub>), 7.33 (d,  $J = 8.0$  Hz, 1H, ArH), 7.41 (d,  $J = 8.4$  Hz, 2H, ArH), 7.55 (d,  $J = 8.4$  Hz, 2H, ArH), 8.22 (d,  $J = 8.8$  Hz, 2H, ArH); IR (KBr),  $\nu$ : 3460, 3322, 2958, 2870, 2184, 1642, 1620, 1567, 1512, 1413, 1372, 1343, 1257, 1146, 1108, 1043, 1021, 871, 827, 754, 669.

Anal. Calcd for C<sub>25</sub>H<sub>24</sub>N<sub>4</sub>O<sub>3</sub>: C 70.08, H 5.65, N 13.08; found C 70.01, H 5.73, N 13.18.

**Ethyl 2-amino-4-(3-chlorophenyl)-7,7-dimethyl-1-(4-methylphenyl)-5-oxo-1,4,5,6,7,8-hexahydroquinolin-3-carboxylate 3l**

Mp 219-221 °C; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>):  $\delta$  0.68 (s, 3H, CH<sub>3</sub>), 0.88 (s, 3H, CH<sub>3</sub>), 1.13 (t,  $J = 7.2$  Hz, 3H, CH<sub>3</sub>), 1.67 (d,  $J = 17.6$  Hz, 1H, CH), 1.98 (d,  $J = 16.0$  Hz, 1H, CH), 2.19 (d,  $J = 16.0$  Hz, 1H, CH), 2.23 (d,  $J = 17.6$  Hz, 1H, CH), 2.42 (s, 3H, CH<sub>3</sub>), 3.97 (q,  $J = 7.2$  Hz, 2H, CH<sub>2</sub>), 4.89 (s, 1H, CH), 6.52 (s, 2H, NH<sub>2</sub>), 7.17 (d,  $J = 8.0$  Hz, 1H, ArH), 7.23-7.33 (m, 5H, ArH), 7.44 (d,  $J = 8.0$  Hz, 2H, ArH); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>): 14.6, 21.0, 26.1, 29.5, 32.1, 34.1, 41.1, 49.5, 78.6, 113.4, 125.6, 125.9, 127.6, 129.7, 129.76, 129.82, 130.1, 131.1, 132.3, 133.5, 139.6, 150.7, 153.0, 168.8, 195.0; IR (KBr),  $\nu$ : 3466, 3268, 3052, 2960, 1659, 1632, 1589, 1495, 1373, 1311, 1271, 1250, 1207, 1173, 1094, 1049, 771, 712, 684.

Anal. Calcd for C<sub>27</sub>H<sub>29</sub>ClN<sub>2</sub>O<sub>3</sub>: C 69.74, H 6.29, N 6.02; found C 69.60, H 6.50, N 6.10.

**Ethyl 2-amino-4-(2-chlorophenyl)-7,7-dimethyl-1-(4-methylphenyl)-5-oxo-1,4,5,6,7,8-hexahydroquinolin-3-carboxylate 3m**

Mp 237-239 °C; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>):  $\delta$  0.69 (s, 3H, CH<sub>3</sub>), 0.86 (s, 3H, CH<sub>3</sub>), 1.16 (t,  $J = 7.2$  Hz, 3H, CH<sub>3</sub>), 1.66 (d,  $J = 17.2$  Hz, 1H, CH), 1.90 (d,  $J = 16.0$  Hz, 1H, CH), 2.14 (d,  $J = 16.0$  Hz, 1H, CH), 2.17 (d,  $J = 17.2$  Hz, 1H, CH), 2.43 (s, 3H, CH<sub>3</sub>), 3.91 (q,  $J = 7.2$  Hz, 2H, CH<sub>2</sub>), 5.20 (s, 1H, CH), 6.70 (s, 2H, NH<sub>2</sub>), 7.08-7.11 (m, 1H, ArH), 7.22-7.26 (m, 2H, ArH), 7.33 (d,  $J = 8.4$  Hz, 2H, ArH), 7.43-7.48 (m, 3H, ArH); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>): 14.6, 21.0, 26.1, 29.5, 31.9, 33.8, 41.4, 49.6, 78.0, 112.6, 126.6, 127.2, 129.3, 130.0, 130.1, 131.0, 132.3, 132.4, 133.5, 139.5, 145.2, 150.6, 153.1, 169.2, 194.7; IR (KBr),  $\nu$ : 3470, 3245, 3061, 2957, 2902, 2868, 1661, 1632, 1589, 1501, 1439, 1371, 1311, 1271, 1250, 1207, 1171, 1144, 1088, 1047, 846, 795, 753, 724.

Anal. Calcd for C<sub>27</sub>H<sub>29</sub>ClN<sub>2</sub>O<sub>3</sub>: C 69.74, H 6.29, N 6.02; found C 69.62, H 6.40, N 6.18.

**Ethyl 2-amino-4-(4-chlorophenyl)-7,7-dimethyl-1-(4-methylphenyl)-5-oxo-1,4,5,6,7,8-hexahydroquinolin-3-carboxylate 3n**

Mp 198-200 °C; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>):  $\delta$  0.67 (s, 3H, CH<sub>3</sub>), 0.87 (s, 3H, CH<sub>3</sub>), 1.12 (t,  $J = 6.8$  Hz, 3H, CH<sub>3</sub>), 1.67 (d,  $J = 17.6$  Hz, 1H, CH), 1.96 (d,  $J = 16.0$  Hz, 1H, CH), 2.18 (d,  $J = 16.0$  Hz, 1H, CH), 2.20 (d,  $J = 17.6$  Hz, 1H, CH), 2.42 (s, 3H, CH<sub>3</sub>), 3.95 (q,  $J = 6.8$  Hz, 2H, CH<sub>2</sub>), 4.90 (s, 1H, CH), 6.74 (s, 2H, NH<sub>2</sub>), 7.29-7.31 (m, 6H, ArH), 7.43 (d,  $J = 8.0$  Hz, 2H, ArH); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>): 14.6, 21.0, 26.1, 29.5, 32.1, 33.6, 41.1, 49.6, 78.7, 113.7, 127.9, 128.9, 129.4, 129.9, 130.1, 131.0, 133.5, 139.5, 147.3, 150.4, 153.0, 168.8, 195.0; IR (KBr),  $\nu$ : 3470, 3247, 3050, 2958, 1666, 1637, 1500, 1372, 1309, 1270, 1251, 1171, 1149, 1087, 1049, 1015, 839, 815.

Anal. Calcd for C<sub>27</sub>H<sub>29</sub>ClN<sub>2</sub>O<sub>3</sub>: C 69.74, H 6.29, N 6.02; found C 69.68, H 6.39, N 6.01.

**Ethyl 2-amino-4-(2,4-dichlorophenyl)-7,7-dimethyl-1-(4-methylphenyl)-5-oxo-1,4,5,6,7,8-hexahydroquinolin-3-carboxylate 3o**

Mp 220-222 °C; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>):  $\delta$  0.68 (s, 3H, CH<sub>3</sub>), 0.84 (s, 3H, CH<sub>3</sub>), 1.05 (t,  $J = 7.2$  Hz, 3H, CH<sub>3</sub>), 1.64 (d,  $J = 17.2$  Hz, 1H, CH), 1.89 (d,  $J = 16.0$  Hz, 1H, CH), 2.15 (d,  $J = 16.0$  Hz, 1H, CH), 2.16 (d,  $J = 17.2$  Hz, 1H, CH), 2.41 (s, 3H, CH<sub>3</sub>), 3.90 (q,  $J = 7.2$  Hz, 2H, CH<sub>2</sub>), 5.15

(s, 1H, CH), 6.70 (s, 2H, NH<sub>2</sub>), 7.30-7.34 (m, 3H, ArH), 7.36 (d, *J* = 2.0 Hz, 1H, ArH), 7.42-7.46 (m, 3H, ArH); IR (KBr),  $\nu$ : 3469, 3250, 2958, 1658, 1632, 1558, 1490, 1371, 1310, 1271, 1249, 1208, 1174, 1150, 1095, 1044, 845, 819, 798, 756.

Anal. Calcd for C<sub>27</sub>H<sub>28</sub>Cl<sub>2</sub>N<sub>2</sub>O<sub>3</sub>: C 64.93, H 5.65, N 5.61; found C 64.88, H 5.70, N 5.73.

**Ethyl 2-amino-7,7-dimethyl-1-(4-methylphenyl)-4-(3-nitrophenyl)-5-oxo-1,4,5,6,7,8-hexahydroquinolin-3-carboxylate 3p**

Mp 236-237 °C; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>):  $\delta$  0.67 (s, 3H, CH<sub>3</sub>), 0.89 (s, 3H, CH<sub>3</sub>), 1.12 (t, *J* = 7.2 Hz, 3H, CH<sub>3</sub>), 1.71 (d, *J* = 17.2 Hz, 1H, CH), 1.97 (d, *J* = 16.0 Hz, 1H, CH), 2.19-2.28 (m, 2H, 2CH), 2.43 (s, 3H, CH<sub>3</sub>), 3.96 (q, *J* = 7.2 Hz, 2H, CH<sub>2</sub>), 5.01 (s, 1H, CH), 6.80 (s, 2H, NH<sub>2</sub>), 7.33 (d, *J* = 8.0 Hz, 2H, ArH), 7.46 (d, *J* = 8.0 Hz, 2H, ArH), 7.57-7.60 (m, 1H, ArH), 7.75 (d, *J* = 7.6 Hz, 1H, ArH), 8.00 (dd, *J* = 8.0 Hz, *J'* = 1.6 Hz, 1H, ArH), 8.12 (d, *J* = 1.6 Hz, 1H, ArH); IR (KBr),  $\nu$ : 3444, 3286, 2961, 1661, 1632, 1529, 1493, 1373, 1348, 1309, 1270, 1206, 1176, 1095, 1042, 900, 821, 794, 744, 722, 702.

Anal. Calcd for C<sub>27</sub>H<sub>29</sub>N<sub>3</sub>O<sub>5</sub>: C 68.19, H 6.15, N 8.84; found C 68.25, H 6.29, N 8.95.

**Methyl 2-amino-7,7-dimethyl-1-(4-methylphenyl)-4-(3-nitrophenyl)-5-oxo-1,4,5,6,7,8-hexahydroquinolin-3-carboxylate 3q**

Mp 256-258 °C; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>):  $\delta$  0.66 (s, 3H, CH<sub>3</sub>), 0.87 (s, 3H, CH<sub>3</sub>), 1.67 (d, *J* = 17.2 Hz, 1H, CH), 1.98 (d, *J* = 16.0 Hz, 1H, CH), 2.20-2.28 (m, 2H, 2CH), 2.42 (s, 3H, CH<sub>3</sub>), 3.54 (s, 3H, CH<sub>3</sub>), 5.03 (s, 1H, CH), 6.84 (s, 2H, NH<sub>2</sub>), 7.31 (d, *J* = 8.0 Hz, 2H, ArH), 7.45 (d, *J* = 8.0 Hz, 1H, ArH), 7.56-7.60 (m, 1H, ArH), 7.74 (d, *J* = 8.0 Hz, 1H, ArH), 8.00 (dd, *J* = 8.4 Hz, *J'* = 1.6 Hz, 1H, ArH), 8.10 (d, *J* = 1.6 Hz, 1H, ArH); IR (KBr),  $\nu$ : 3456, 3272, 2954, 1687, 1663, 1634, 1523, 1496, 1435, 1371, 1347, 1324, 1270, 1252, 1210, 1175, 1149, 1082, 923, 825, 806, 780, 747, 725, 701.

Anal. Calcd for C<sub>26</sub>H<sub>27</sub>N<sub>3</sub>O<sub>5</sub>: C 67.66, H 5.90, N 9.10; found C 67.54, H 6.09, N 9.22.

**Ethyl 2-amino-4-(4-chlorophenyl)-7,7-dimethyl-5-oxo-1-phenyl-1,4,5,6,7,8-hexahydroquinolin-3-carboxylate 3r**

Mp 204-206 °C; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>):  $\delta$  0.66 (s, 3H, CH<sub>3</sub>), 0.86 (s, 3H, CH<sub>3</sub>), 1.12 (t, *J* = 6.8 Hz, 3H, CH<sub>3</sub>), 1.62 (d, *J* = 17.6 Hz, 1H, CH), 1.97 (d, *J* = 16.0 Hz, 1H, CH),

2.19 (d, *J* = 16.0 Hz, 1H, CH), 2.22 (d, *J* = 17.6 Hz, 1H, CH), 3.95 (q, *J* = 6.8 Hz, 2H, CH<sub>2</sub>), 4.90 (s, 1H, CH), 6.73 (s, 2H, NH<sub>2</sub>), 7.30 (s, 4H, ArH), 7.42 (d, *J* = 6.8 Hz, 2H, ArH), 7.59-7.65 (m, 3H, ArH); IR (KBr),  $\nu$ : 3384, 3270, 2962, 1652, 1640, 1591, 1488, 1411, 1373, 1306, 1269, 1247, 1209, 1170, 1148, 1119, 1083, 1040, 1012, 846, 784, 755, 704.

Anal. Calcd for C<sub>26</sub>H<sub>27</sub>ClN<sub>2</sub>O<sub>3</sub>: C 69.25, H 6.03, N 6.21; found C 69.10, H 6.21, N 6.25.

**Ethyl 2-amino-4-(3-chlorophenyl)-7,7-dimethyl-1-(4-fluorophenyl)-5-oxo-1,4,5,6,7,8-hexahydroquinolin-3-carboxylate 3s**

Mp 226-228 °C; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>):  $\delta$  0.67 (s, 3H, CH<sub>3</sub>), 0.89 (s, 3H, CH<sub>3</sub>), 1.12 (t, *J* = 6.8 Hz, 3H, CH<sub>3</sub>), 1.69 (d, *J* = 17.2 Hz, 1H, CH), 1.97 (d, *J* = 16.0 Hz, 1H, CH), 2.21 (d, *J* = 16.0 Hz, 1H, CH), 2.26 (d, *J* = 17.2 Hz, 1H, CH), 3.95 (q, *J* = 6.8 Hz, 2H, CH<sub>2</sub>), 5.00 (s, 1H, CH), 6.92 (s, 2H, NH<sub>2</sub>), 7.48-7.52 (m, 4H, ArH), 7.58 (t, *J* = 8.0 Hz, 1H, ArH), 7.75 (d, *J* = 7.6 Hz, 1H, ArH), 8.00 (dd, *J* = 8.0 Hz, *J'* = 1.6 Hz, 1H, ArH), 8.11 (d, *J* = 1.6 Hz, 1H, ArH); IR (KBr),  $\nu$ : 3465, 3275, 2957, 1667, 1627, 1508, 1373, 1349, 1327, 1303, 1271, 1244, 1211, 1177, 1156, 1090, 1045, 927, 897, 861, 782, 728, 700.

Anal. Calcd for C<sub>26</sub>H<sub>26</sub>ClFN<sub>2</sub>O<sub>3</sub>: C 66.59, H 5.59, N 5.97; found C 66.70, H 5.72, N 6.10.

In conclusion, we found a novel method available for the synthesis of 1,4-diarylquinoline derivatives in aqueous media catalyzed by TEBAC in high yields. Meanwhile, the aqueous medium chosen was a green solvent which could be reused for several rounds without significant loss of activity.

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