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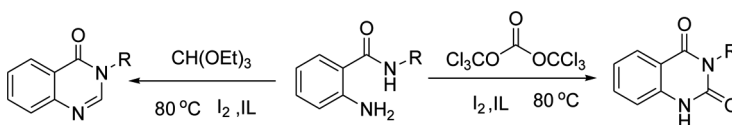
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## GREEN SYNTHESIS OF QUINAZOLINONE DERIVATIVES CATALYZED BY IODINE IN IONIC LIQUID

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### GRAPHICAL ABSTRACT



**Abstract** A series of quinazolinone derivatives were synthesized by the reaction of 2-aminobenzamides and triethyl orthoformate or triphosgene in ionic liquid of [BMIm]BF<sub>4</sub> at 80 °C catalyzed by iodine in good yields. Compared to other methods, this new procedure has the advantages of mild reaction conditions, good yields, operational simplicity, and environmentally friendly procedure.

**Keywords** 2-Aminobenzamides; ionic liquid; quinazolinone; synthesis

## INTRODUCTION

Quinazolinone and its derivatives are important compounds for their wide range of biological activities.<sup>[1]</sup> These include anti-inflammatory,<sup>[2]</sup> antihypertensive,<sup>[3]</sup> anticancer,<sup>[4]</sup> antitumor,<sup>[5]</sup> and antibacterial activity.<sup>[6]</sup> Therefore, the synthesis of quinazolinone derivatives is currently of great interest. Although many methods<sup>[7]</sup> have been reported for the synthesis of quinazolinones in the literature, the known methods are not straightforward and involve various disadvantages, such as poor yields, prolonged reaction times, and the use of toxic organic reagents.

Room-temperature ionic liquids,<sup>[8]</sup> especially those based on the 1-*N*-alkyl-3-methyl imidazolium cation, have attracted much attention in recent years as alternative green reaction media because of their unique chemical and physical properties of nonvolatility, nonflammability, thermal stability, and controlled miscibility. Therefore, room-temperature ionic liquids have found growing applications in organic reactions. Several examples of these reactions include hydrogenations,<sup>[9]</sup>

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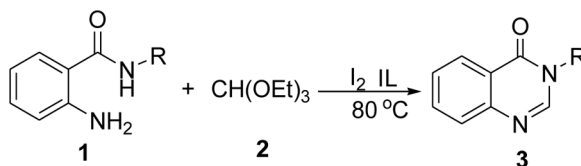
Friedel–Crafts reactions,<sup>[10]</sup> Heck reactions,<sup>[11]</sup> Bishler–Napieralski reactions,<sup>[12]</sup> olefin hydrodimerizations,<sup>[13]</sup> and olefin dimerizations.<sup>[14]</sup>

As a part of a program toward the synthesis of suitably functionalized heterocyclic compounds of potential biological activity in green media,<sup>[15]</sup> herein we report a green synthesis of quinazolinone derivatives by the reaction of 2-aminobenzamides and triethyl orthoformate or triphosgene in ionic liquid of [BMIm]BF<sub>4</sub> catalyzed by iodine at 80 °C.

## RESULTS AND DISCUSSION

When the reaction of 2-aminobenzamides **1** and triethyl orthoformate **2** was performed in ionic liquid of [BMIm]BF<sub>4</sub> at 80 °C in the presence of 5 mol% iodine, good yields of quinazolin-4(3*H*)-one derivatives **3** were obtained (Scheme 1).

At completion as monitored by thin-layer chromatography (TLC), the reaction mixture was allowed to cool to room temperature. A little amount of water was added to the mixture, and the crude product was isolated by filtration. The water in the filtrate was removed by distillation under reduced pressure, and the ionic liquid in the residue was then recovered for reuse by evaporation at 80 °C for several hours in vacuum. Investigations using triethyl orthoformate and 2-aminobenzamide as model substrates showed the successive reuse of the recycled ionic liquid. Even in the fourth round, the yield of the product **3a** is fairly high (89%).



**Scheme 1.** Iodine-catalyzed reactions of **1** and **2** in ionic liquid.

**Table 1.** Synthetic results of **3** in ionic liquid at 80 °C catalyzed by iodine<sup>a</sup>

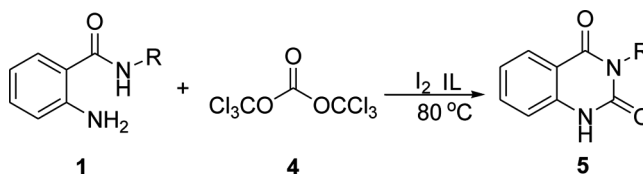
Entry	R	Products	Time (min)	Isolated yields (%)
1	H	<b>3a</b>	40	90
2	4-MeC <sub>6</sub> H <sub>4</sub>	<b>3b</b>	35	93
3	4-MeOC <sub>6</sub> H <sub>4</sub>	<b>3c</b>	30	98
4	4-FC <sub>6</sub> H <sub>4</sub>	<b>3d</b>	50	95
5	C <sub>6</sub> H <sub>5</sub>	<b>3e</b>	45	95
6	C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub>	<b>3f</b>	30	98
7	4-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub>	<b>3g</b>	45	99
8	4- <i>i</i> -PrC <sub>6</sub> H <sub>4</sub>	<b>3h</b>	45	87
9	4-MeC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub>	<b>3i</b>	30	90
10	3,4-OCH <sub>2</sub> OC <sub>6</sub> H <sub>3</sub> CH <sub>2</sub> CH <sub>2</sub>	<b>3j</b>	30	92
11	3- <i>n</i> -Bu	<b>3k</b>	30	98
12	2-FurylCH <sub>2</sub>	<b>3l</b>	30	90

<sup>a</sup>Reaction condition: [BMIm]BF<sub>4</sub> (2 mL), **1** (2 mmol), **2** (0.311 g, 2.1 mmol), iodine (0.026 g, 0.1 mmol), 80 °C.

**Table 2.** Synthetic results of **5** catalyzed by iodine in ionic liquid<sup>a</sup>

Entry	R	Products	Time (min)	Isolated yields (%)
1	H	<b>5a</b>	45	92
2	C <sub>6</sub> H <sub>5</sub>	<b>5b</b>	45	98
3	Cyclohexyl	<b>5c</b>	30	98
4	4-FC <sub>6</sub> H <sub>4</sub>	<b>5d</b>	45	93
5	4-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub>	<b>5e</b>	30	95
6	C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub>	<b>5f</b>	45	90
7	4-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub>	<b>5g</b>	60	92
8	4-MeC <sub>6</sub> H <sub>4</sub>	<b>5h</b>	60	93

<sup>a</sup>Reaction condition: [BMIm]BF<sub>4</sub> (2 mL), **1** (2 mmol), **4** (0.296 g, 1 mmol), iodine (0.026 g, 0.1 mmol), 80 °C.

**Scheme 2.** Iodine-catalyzed reactions of **1** and **4** in ionic liquid.

To demonstrate the efficiency and the applicability of the present method, we performed the reactions of a variety of 2-aminobenzamides **1** with **2** at 80 °C in the presence of iodine in [BMIm]BF<sub>4</sub>. As shown in Table 1, a series of 2-aminobenzamides **1** reacted well with **2** to give the corresponding products **3** in good yields under the same reaction conditions. For aldehyde **1**, the yields of **3** were not sensitive to the electronic properties of the aromatic ring in the presence of electron-withdrawing groups (such as halide) or electron-donating groups (such as alkyl and alkoxyl group) (Table 1).

To obtain quinazoline-2,4(*1H*,*3H*)-dione derivatives, triphosgene **4** was selected to react with 2-aminobenzamides instead of triethyl orthoformate. As expected, 3-substituted quinazoline-2,4(*1H*,*3H*)-diones **5** were isolated in good yields (Table 2) in the same reaction conditions (Scheme 2).

## CONCLUSION

In conclusion, we found a green method for the syntheses of quinazolinone derivatives by the reactions of 2-aminobenzamides and triethyl orthoformate or triphosgene at 80 °C in ionic liquid catalyzed by iodine. The features of this procedure are mild reaction conditions, good yields, operational simplicity, and environmentally friendly procedure. Meanwhile, [BMIm]BF<sub>4</sub> could be reused for several rounds without significant loss of activity.

## EXPERIMENTAL

Melting points were determined in open capillaries and are uncorrected. Infrared (IR) spectra were recorded on a Tensor 27 spectrometer in KBr. <sup>1</sup>H NMR

spectra were obtained from solution in dimethylsulfoxide (DMSO- $d_6$ ) with Me<sub>4</sub>Si as internal standard using a Bruker-400 spectrometer. High-resolution mass spectrographic (HRMS) analyses were carried out using a Bruker-micro-TOF-Q-MS analyzer.

### General Procedure for the Syntheses of Quinazolin-4(3*H*)-one Derivatives

A dry 50-mL flask was charged with triethyl orthoformate (0.311 g, 2.1 mmol), 2-aminobenzamides (2.0 mmol), and ionic liquid of [BMIm]BF<sub>4</sub> (2 mL). The reaction mixture was stirred at 80 °C for 30–50 min and then cooled to room temperature. A little amount of water (5 mL) was added to the mixture, and the generated solid was filtered off. The water in the filtrate was removed by distillation under reduced pressure, and the ionic liquid in the residue was then recovered for reuse by evaporating at 80 °C for 4 h in a vacuum. The crude yellow products were washed with water and purified by recrystallization from 95% EtOH to give **3**.

### Selected Data

**Quinazolin-4(3*H*)-one 3a.** Mp 212–214 °C. <sup>1</sup>H NMR (DMSO- $d_6$ , 400 MHz):  $\delta_{\text{H}}$  7.51–7.55 (m, 1H, ArH), 7.67 (d,  $J$  = 8.4 Hz, 1H, ArH), 7.80–7.84 (m, 1H, ArH), 8.11–8.14 (m, 2H, ArH + CH), 12.25 (s, 1H, NH); IR (KBr): 3134, 3043, 1704, 1666, 1611, 1468, 1388, 1326, 1255, 1234, 1170, 921, 826, 807, 764, 684 cm<sup>-1</sup>. HRMS (ESI,  $m/z$ ): calcd. for C<sub>8</sub>H<sub>6</sub>N<sub>2</sub>O<sub>2</sub>Na (M + Na<sup>+</sup>) 169.0378; found 169.0382.

**3-*p*-Tolylquinazolin-4(3*H*)-one 3b.** Mp 144–145 °C (lit.<sup>[7k]</sup> 146–147 °C). <sup>1</sup>H NMR (DMSO- $d_6$ , 400 MHz):  $\delta_{\text{H}}$  2.39 (s, 3H, CH<sub>3</sub>), 7.36 (d,  $J$  = 8.0 Hz, 1H, ArH), 7.42 (d,  $J$  = 8.0 Hz, 2H, ArH), 7.57–7.61 (m, 1H, ArH), 7.74 (d,  $J$  = 8.0 Hz, 1H, ArH), 7.86–7.90 (m, 1H, ArH), 8.20 (dd,  $J$  = 8.0 Hz,  $J$  = 0.8 Hz, 1H, ArH), 8.32 (s, 1H, CH); IR (KBr): 3032, 2915, 1691, 1642, 1599, 1564, 1513, 1471, 1407, 1324, 1293, 1259, 1190, 1112, 917, 816, 771, 749, 694 cm<sup>-1</sup>. HRMS (ESI,  $m/z$ ): Calcd. for C<sub>15</sub>H<sub>12</sub>N<sub>2</sub>O<sub>2</sub>Na (M + Na<sup>+</sup>) 259.0847; found 259.0852.

**3-(4-Methoxyphenyl)quinazolin-4(3*H*)-one 3c.** Mp 193–194 °C (lit.<sup>[7k]</sup> 189–191 °C). <sup>1</sup>H NMR (DMSO- $d_6$ , 400 MHz):  $\delta_{\text{H}}$  3.84 (s, 3H, OCH<sub>3</sub>), 7.10 (d,  $J$  = 8.8 Hz, 2H, ArH), 7.47 (d,  $J$  = 8.8 Hz, 2H, ArH), 7.58–7.62 (m, 1H, ArH), 7.74 (d,  $J$  = 8.0 Hz, 1H, ArH), 7.86–7.90 (m, 1H, ArH), 8.20 (d,  $J$  = 7.6 Hz, 1H, ArH), 8.31 (s, 1H, CH); IR (KBr): 3044, 2955, 1682, 1613, 1565, 1516, 1470, 1442, 1414, 1324, 1288, 1264, 1214, 1181, 1113, 1036, 917, 831, 769, 750, 694 cm<sup>-1</sup>. HRMS (ESI,  $m/z$ ): calcd. for C<sub>15</sub>H<sub>12</sub>N<sub>2</sub>O<sub>2</sub>Na (M + Na<sup>+</sup>) 275.0796; found 275.0788.

**3-(4-Fluorophenyl)quinazolin-4(3*H*)-one 3d.** Mp 204–206 °C. <sup>1</sup>H NMR (DMSO- $d_6$ , 400 MHz):  $\delta_{\text{H}}$  7.12 (d,  $J$  = 8.8 Hz, 2H, ArH), 7.45 (d,  $J$  = 8.8 Hz, 2H, ArH), 7.60 (t,  $J$  = 7.6 Hz, 1H, ArH), 7.74 (d,  $J$  = 8.8 Hz, 1H, ArH), 7.88 (t,  $J$  = 7.6 Hz, 1H, ArH), 8.20 (d,  $J$  = 7.6 Hz, 1H, ArH), 8.31 (s, 1H, CH); IR (KBr): 3067, 1665, 1611, 1564, 1511, 1469, 1419, 1405, 1327, 1293, 1261, 1225, 1185, 1161, 1143, 1113, 1019, 927, 914, 774, 751, 696 cm<sup>-1</sup>. HRMS (ESI,  $m/z$ ): calcd. for C<sub>14</sub>H<sub>9</sub>FN<sub>2</sub>O<sub>2</sub>Na (M + Na<sup>+</sup>) 263.0597; found 263.0594.

**3-Phenylquinazolin-4(3H)-one 3e.** Mp 141–142 °C (lit.<sup>[7k]</sup> 139–140 °C). <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 400 MHz): δ<sub>H</sub> 7.52–7.63 (m, 6H, ArH), 7.76 (d, *J* = 8.0 Hz, 1H, ArH), 7.88–7.92 (m, 1H, ArH), 8.22 (dd, *J* = 8.0 Hz, *J'* = 0.8 Hz, 1H, ArH), 8.36 (s, 1H, CH); IR (KBr): 3050, 2938, 1728, 1666, 1608, 1589, 1478, 1443, 1393, 1328, 1297, 1265, 1238, 1158, 1070, 1024, 918, 772, 748, 700 cm<sup>−1</sup>. HRMS (ESI, *m/z*): calcd. for C<sub>14</sub>H<sub>10</sub>N<sub>2</sub>ONa (M + Na<sup>+</sup>) 245.0691; found 245.0683.

**3-Benzylquinazolin-4(3H)-one 3f.** Mp 119–120 °C (lit.<sup>[7k]</sup> 117–118 °C). <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 400 MHz): δ<sub>H</sub> 5.21 (s, 2H, CH<sub>2</sub>), 7.26–7.39 (m, 5H, ArH), 7.52–7.56 (m, 1H, ArH), 7.70 (d, *J* = 8.0 Hz, 1H, ArH), 7.80–7.84 (m, 1H, ArH), 8.16 (dd, *J* = 8.0 Hz, *J'* = 0.8 Hz, 1H, ArH), 8.60 (s, 1H, CH); IR (KBr): 3065, 3036, 2988, 2945, 1678, 1606, 1561, 1474, 1441, 1412, 1366, 1319, 1257, 1226, 1209, 1149, 1102, 1076, 1025, 938, 915, 869, 776, 747, 701, 691 cm<sup>−1</sup>. HRMS (ESI, *m/z*): calcd. for C<sub>15</sub>H<sub>12</sub>N<sub>2</sub>ONa (M + Na<sup>+</sup>) 259.0847, found 259.0856.

**3-(4-Methoxybenzyl)quinazolin-4(3H)-one 3g.** Mp 134–135 °C. <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 400 MHz): δ<sub>H</sub> 3.72 (s, 3H, OCH<sub>3</sub>), 5.13 (s, 2H, CH<sub>2</sub>), 6.90 (d, *J* = 8.8 Hz, 2H, ArH), 7.36 (d, *J* = 8.8 Hz, 2H, ArH), 7.55 (t, *J* = 7.6 Hz, 1H, ArH), 7.68 (d, *J* = 8.0 Hz, 1H, ArH), 7.80–7.84 (m, 1H, ArH), 8.16 (dd, *J* = 8.0 Hz, *J'* = 0.8 Hz, 1H, ArH), 8.58 (s, 1H, CH); IR (KBr): 3058, 3001, 2956, 2913, 2837, 1665, 1610, 1563, 1513, 1471, 1368, 1323, 1293, 1245, 1184, 1165, 1103, 1026, 959, 817, 769, 694 cm<sup>−1</sup>. HRMS (ESI, *m/z*): calcd. for C<sub>16</sub>H<sub>14</sub>N<sub>2</sub>O<sub>2</sub>Na (M + Na<sup>+</sup>) 289.0953; found 289.0964.

**3-(4-*i*-Propylphenyl)quinazolin-4(3H)-one 3h.** Mp 126–127 °C. <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 400 MHz): δ<sub>H</sub> 1.27 (d, *J* = 2.8 Hz, 6H, 2CH<sub>3</sub>), 2.97–3.04 (m, 1H, CH), 7.43–7.47 (m, 4H, ArH), 7.61 (t, *J* = 7.6 Hz, 1H, ArH), 7.74–7.60 (m, 1H, ArH), 7.87–7.91 (m, 1H, ArH), 8.21 (d, *J* = 7.6 Hz, 1H, ArH), 8.35 (s, 1H, CH); IR (KBr): 3051, 2960, 2925, 2870, 1680, 1614, 1598, 1562, 1509, 1473, 1423, 1324, 1294, 1257, 1185, 1112, 1022, 913, 845, 816, 771, 696 cm<sup>−1</sup>. HRMS (ESI, *m/z*): calcd. for C<sub>17</sub>H<sub>16</sub>N<sub>2</sub>NaO (M + Na<sup>+</sup>) 287.1160; found 287.1167.

**3-(4-Methylbenzyl)quinazolin-4(3H)-one 3i.** Mp 133–135 °C. <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 400 MHz): δ<sub>H</sub> 2.26 (s, 3H, CH<sub>3</sub>), 5.16 (s, 2H, CH<sub>2</sub>), 7.15 (d, *J* = 8.0 Hz, 2H, ArH), 7.27 (d, *J* = 8.0 Hz, 2H, ArH), 7.56 (t, *J* = 7.6 Hz, 1H, ArH), 7.67 (d, *J* = 8.0 Hz, 1H, ArH), 7.84 (t, *J* = 7.2 Hz, 1H, ArH), 8.16 (d, *J* = 8.0 Hz, 1H, ArH), 8.56 (s, 1H, CH); IR (KBr): 3030, 2985, 2942, 2922, 2861, 1672, 1607, 1563, 1517, 1471, 1360, 1321, 1291, 1254, 1173, 1154, 1101, 942, 782, 699, 573 cm<sup>−1</sup>. HRMS (ESI, *m/z*): calcd. for C<sub>16</sub>H<sub>14</sub>N<sub>2</sub>NaO (M + Na<sup>+</sup>) 273.1004; found 273.1015.

**3-(2-(3,4-Methylenedioxyphenyl)ethyl)quinazolin-4(3H)-one 3j.** Mp 129–130 °C. <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 400 MHz): δ<sub>H</sub> 2.94 (t, *J* = 7.2 Hz, 2H, CH<sub>2</sub>), 4.18 (t, *J* = 7.2 Hz, 2H, CH<sub>2</sub>), 5.98 (s, 2H, CH<sub>2</sub>), 6.22 (d, *J* = 8.0 Hz, 1H, ArH), 6.80 (d, *J* = 8.0 Hz, 1H, ArH), 6.87 (s, 1H, ArH), 7.56 (t, *J* = 7.6 Hz, 1H, ArH), 7.65 (d, *J* = 8.0 Hz, 1H, ArH), 7.80–7.84 (m, 1H, ArH), 8.15 (s, 1H, CH), 8.18 (d, *J* = 8.0 Hz, 1H, ArH); IR (KBr): 3056, 2977, 2947, 2898, 2777, 1665, 1612, 1561, 1504, 1488, 1443, 1366, 1326, 1270, 1245, 1202, 1156, 1041, 926, 879, 856, 774, 701, 606 cm<sup>−1</sup>. HRMS (ESI, *m/z*): calcd. for C<sub>17</sub>H<sub>14</sub>N<sub>2</sub>NaO<sub>3</sub> (M + Na<sup>+</sup>) 317.0902; found 317.0921.

**3-(*n*-Butyl)quinazolin-4(3H)-one 3k.** Mp 70–72 °C. <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 400 MHz): δ<sub>H</sub> 0.92 (t, *J* = 7.6 Hz, 3H, CH<sub>3</sub>), 1.29–1.35 (m, 2H, CH<sub>2</sub>), 1.64–1.72

(m, 2H, CH<sub>2</sub>), 3.98 (t,  $J=7.6$  Hz, 2H, CH<sub>2</sub>), 7.53–7.57 (m, 1H, ArH), 7.68 (d,  $J=8.0$  Hz, 1H, ArH), 7.81–7.85 (m, 1H, ArH), 8.16 (d,  $J=8.0$  Hz, 1H, ArH), 8.40 (s, 1H, CH); IR (KBr): 3061, 2955, 2930, 2869, 1670, 1612, 1561, 1472, 1372, 1326, 1289, 1256, 1175, 1143, 1107, 937, 876, 768, 696 cm<sup>-1</sup>. HRMS (ESI,  $m/z$ ): calcd. for C<sub>12</sub>H<sub>14</sub>N<sub>2</sub>NaO ( $M + Na^+$ ) 225.1004; found 225.1010.

**3-((Furan-2-yl)methyl)quinazolin-4(3H)-one 3l.** Mp 128–129 °C. <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 400 MHz): δ<sub>H</sub> 5.24 (s, 2H, CH<sub>2</sub>), 6.43–6.48 (m, 2H, ArH), 7.55–7.58 (m, 1H, ArH), 7.62 (s, 1H, ArH), 7.68–7.71 (m, 1H, ArH), 7.82–7.86 (m, 1H, ArH), 8.16 (d,  $J=8.0$  Hz, 1H, ArH), 8.49 (s, 1H, CH); IR (KBr): 3105, 3069, 3053, 2938, 1671, 1612, 1561, 1499, 1474, 1355, 1318, 1261, 1178, 1157, 951, 775, 759, 689, 601 cm<sup>-1</sup>. HRMS (ESI,  $m/z$ ): calcd. for C<sub>13</sub>H<sub>10</sub>N<sub>2</sub>NaO<sub>2</sub> ( $M + Na^+$ ) 249.0640; found 249.0655.

### General Procedure for the Syntheses of 3-Substituted Quinazoline-2,4(1H,3H)-diones

A dry 50-mL flask was charged with triphosgene (1.0 mmol), 2-aminobenzamides (2.0 mmol), and ionic liquid of [BMIm]BF<sub>4</sub> (2 mL). The reaction mixture was stirred at 80 °C for 30–60 min and then cooled to room temperature. A little amount of water (5 mL) was added to the mixture, and the generated solid was filtered off. The water in the filtrate was removed by distillation under reduced pressure, and the ionic liquid in the residue was then recovered by evaporating at 80 °C for 4 h in a vacuum. The crude yellow products were washed with water and purified by recrystallization from 95% EtOH to give **5**.

### Selected Data

**Quinazoline-2,4(1H,3H)-dione 5a.** Mp >300 °C (lit.<sup>[71]</sup> >300 °C). <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 400 MHz): δ<sub>H</sub> 7.16–7.20 (m, 2H, ArH), 7.62–7.66 (m, 1H, ArH), 7.89 (d,  $J=7.6$  Hz, 1H, ArH), 11.16 (s, 1H, NH), 11.30 (s, 1H, NH); IR (KBr): 3210, 3165, 3056, 1704, 1662, 1618, 1506, 1484, 1444, 1405, 1300, 1141, 1039, 859, 779, 757, 684 cm<sup>-1</sup>.

**3-Phenylquinazoline-2,4(1H,3H)-dione 5b.** Mp 280–282 °C (lit.<sup>[7m]</sup> 280–282 °C). <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 400 MHz): (δ<sub>H</sub> 7.22–7.25 (m, 2H, ArH), 7.33 (d,  $J=6.8$  Hz, 2H, ArH), 7.41–7.45 (m, 1H, ArH), 7.47–7.51 (m, 2H, ArH), 7.69–7.73 (m, 1H, ArH), 7.95 (d,  $J=7.6$  Hz, 1H, ArH), 11.57 (s, 1H, NH); IR (KBr): 3198, 3072, 3008, 1728, 1659, 1611, 1492, 1448, 1402, 1341, 1289, 1242, 1151, 868, 821, 782, 755, 707, 685 cm<sup>-1</sup>.

**3-Cyclohexylquinazoline-2,4(1H,3H)-dione 5c.** Mp 272–273 °C (lit.<sup>[7m]</sup> 270–271 °C). <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 400 MHz): δ<sub>H</sub> 1.13–1.19 (m, 1H), 1.25–1.35 (m, 2H, CH<sub>2</sub>), 1.57–1.64 (m, 3H, CH<sub>2</sub>+CH), 1.80 (d, 2H,  $J=12.8$  Hz, 2H, CH<sub>2</sub>), 2.34–2.43 (m, 2H, CH<sub>2</sub>), 4.70–4.76 (m, 1H, CH), 7.12–7.19 (m, 2H, ArH), 7.60–7.64 (m, 1H, ArH), 7.90 (d,  $J=8.0$  Hz, 1H, ArH), 11.32 (s, 1H, NH); IR (KBr): 3228, 2930, 2860, 1716, 1640, 1505, 1448, 1400, 1378, 1348, 1279, 1262, 1182, 1157, 1113, 1004, 895, 746, 689 cm<sup>-1</sup>.



**3-(4-Fluorophenyl)quinazoline-2,4(1H,3H)-dione 5d.** Mp 270–272 °C.  $^1\text{H}$  NMR (DMSO- $d_6$ , 400 MHz):  $\delta_{\text{H}}$  7.22–7.25 (m, 2H, ArH), 7.32 (t,  $J=8.8$  Hz, 2H, ArH), 7.39 (t,  $J=8.8$  Hz, 2H, ArH), 7.69–7.73 (m, 1H, ArH), 7.94 (d,  $J=7.6$  Hz, 1H, ArH), 11.59 (s, 1H, NH); IR (KBr): 3205, 1730, 1651, 1602, 1508, 1440, 1402, 13442, 1275, 1243, 1213, 1169, 840, 811, 761, 718, 690  $\text{cm}^{-1}$ . HRMS (ESI,  $m/z$ ): calcd. for  $\text{C}_{14}\text{H}_9\text{FN}_2\text{O}_2\text{Na}$  ( $\text{M} + \text{Na}^+$ ) 279.0546; found 279.0536.

**3-(4-Methoxyphenyl)quinazoline-2,4(1H,3H)-dione 5e.** Mp > 300 °C.  $^1\text{H}$  NMR (DMSO- $d_6$ , 400 MHz):  $\delta_{\text{H}}$  3.81 (s, 3H,  $\text{CH}_3\text{O}$ ), 7.02 (d,  $J=8.8$  Hz, 2H, ArH), 7.20–7.24 (m, 4H, ArH), 7.68–7.71 (m, 1H, ArH), 7.94 (d,  $J=7.6$  Hz, 1H, ArH), 11.52 (s, 1H, NH); IR (KBr): 3196, 3068, 3002, 2933, 2896, 1722, 1662, 1606, 1513, 1489, 1448, 1405, 1284, 1247, 1175, 1156, 1029, 826, 791, 760, 670  $\text{cm}^{-1}$ . HRMS (ESI,  $m/z$ ): calcd. for  $\text{C}_{15}\text{H}_{12}\text{N}_2\text{O}_3\text{Na}$  ( $\text{M} + \text{Na}^+$ ) 291.0746; found 291.0771.

**3-Benzylquinazoline-2,4(1H,3H)-dione 5f.** Mp 233–234 °C.  $^1\text{H}$  NMR (DMSO- $d_6$ , 400 MHz):  $\delta_{\text{H}}$  5.10 (s, 2H,  $\text{CH}_2$ ), 7.20–7.26 (m, 3H, ArH), 7.29–7.32 (m, 4H, ArH), 7.66–7.70 (m, 1H, ArH), 7.95 (d,  $J=8.0$  Hz, 1H, ArH), 11.55 (s, 1H, NH); IR (KBr): 3191, 3054, 3003, 2905, 1712, 1654, 1491, 1453, 1427, 1410, 1353, 1301, 1072, 956, 815, 755, 714  $\text{cm}^{-1}$ . HRMS (ESI,  $m/z$ ): calcd. for  $\text{C}_{15}\text{H}_{12}\text{N}_2\text{O}_2\text{Na}$  ( $\text{M} + \text{Na}^+$ ) 275.0796; found 275.0782.

**3-(4-Methoxybenzyl)quinazoline-2,4(1H,3H)-dione 5g.** Mp 219–220 °C.  $^1\text{H}$  NMR (DMSO- $d_6$ , 400 MHz):  $\delta_{\text{H}}$  3.70 (s, 3H,  $\text{OCH}_3$ ), 5.02 (s, 2H,  $\text{CH}_2$ ), 6.86 (d,  $J=8.4$  Hz, 2H, ArH), 7.18–7.21 (m, 2H, ArH), 7.29 (d,  $J=8.4$  Hz, 2H, ArH), 7.62–7.66 (m, 1H, ArH), 7.93 (d,  $J=8.0$  Hz, 1H, ArH), 11.51 (s, 1H, NH); IR (KBr): 3057, 3004, 2905, 1716, 1663, 1609, 1511, 1454, 1429, 1413, 1352, 1306, 1247, 1174, 1098, 1031, 958, 822, 754  $\text{cm}^{-1}$ . HRMS (ESI,  $m/z$ ): calcd. for  $\text{C}_{16}\text{H}_{14}\text{N}_2\text{O}_3\text{Na}$  ( $\text{M} + \text{Na}^+$ ) 305.0902; found 305.0908.

**3-*p*-Tolylquinazoline-2,4(1H,3H)-dione 5h.** Mp 269–270 °C. (lit.<sup>[7m]</sup> 265–266 °C).  $^1\text{H}$  NMR (DMSO- $d_6$ , 400 MHz):  $\delta_{\text{H}}$  2.38 (s, 3H,  $\text{CH}_3$ ), 7.19 (d,  $J=8.0$  Hz, 2H, ArH), 7.23 (d,  $J=7.6$  Hz, 2H, ArH), 7.28 (d,  $J=8.0$  Hz, 2H, ArH), 7.68–7.72 (m, 1H, ArH), 7.94 (d,  $J=8.0$  Hz, 1H, ArH), 11.54 (s, 1H, NH); IR (KBr): 3197, 3069, 3006, 2937, 1722, 1665, 1621, 1607, 1512, 1489, 1447, 1404, 1287, 1243, 1154, 872, 817, 754, 715, 671  $\text{cm}^{-1}$ .

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