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## EFFICIENT SYNTHESIS OF QUINAZOLINE-2,4(1*H*,3*H*)-DIONES FROM 2-AMINOBENZONITRILES AND CO<sub>2</sub> CATALYZED BY 2-HYDROXYPYRIDINE ANION-BASED IONIC LIQUID AT ATMOSPHERIC PRESSURE

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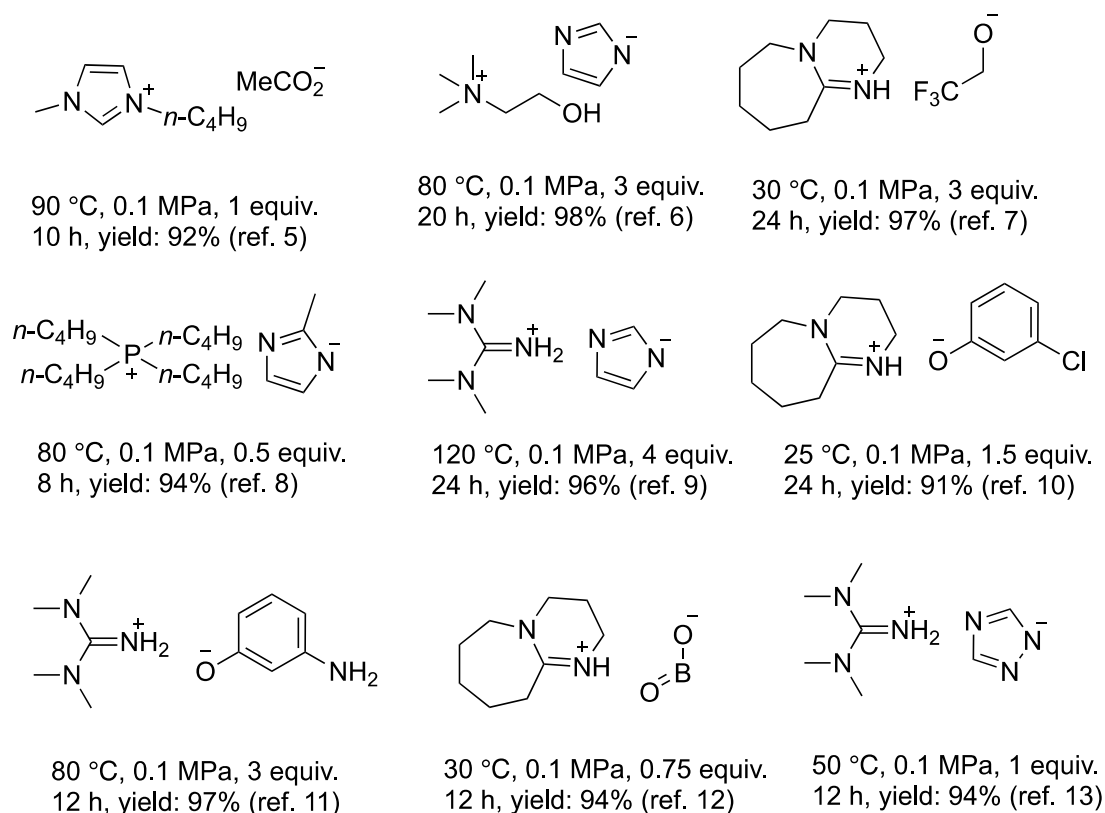
**Abstract** – Ionic liquids are widely used in the capture and utilization of CO<sub>2</sub>, and achieving efficient chemical conversion of CO<sub>2</sub> under atmospheric pressure remains a challenging research topic. In this paper, 2-hydroxypyridine anion-based ionic liquids, which were easy to prepare, were used to synthesize quinazoline-2,4(1*H*,3*H*)-diones from 2-aminobenzonitriles and CO<sub>2</sub> at atmospheric pressure. The reaction sequence worked well for 4-substituted substrates, but the effect was poor for 3-substituted substrates, possibly due to steric hindrance. The CO<sub>2</sub> absorption experiment and <sup>13</sup>C NMR analysis show that [Ch][2-OP]-CO<sub>2</sub> complex is the actual catalyst for this reaction. This method has moderate to excellent yields for catalytic conversion of various 4-substituted 2-aminobenzonitriles with electron withdrawing and electron donating groups, providing a new way for chemical conversion and utilization of CO<sub>2</sub>.

Ionic liquids (ILs), due to their unique properties, have become a favorable media in CO<sub>2</sub> capture and utilization (CCU) processes. The chemical structures and physical properties of ILs could be changed by selecting specific functional cations or anions, and the application of ILs in CCU could also be modified correspondingly.<sup>1</sup> ILs can be act as solvent, CO<sub>2</sub> absorbents, CO<sub>2</sub> activating or catalyst in the conversion of CO<sub>2</sub> to value-added products.<sup>2,3</sup>

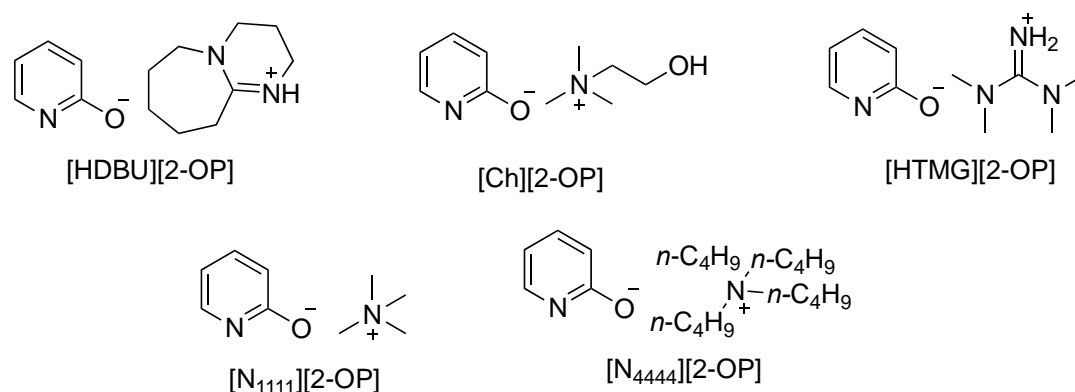
Quinazoline-2,4(1*H*,3*H*)-diones serve as an important class of intermediates with multiple biological and pharmacological activities.<sup>4</sup> Compared with traditional synthetic methods, the atom-economical synthesis of these compounds from CO<sub>2</sub> and 2-aminobenzonitriles shows great advantage, and it has been widely

investigated using various ILs at atmospheric pressure as shown in **Figure 1**.<sup>5-13</sup> The functional ions in these ILs are selected from imidazole, triazole, tetramethylguanidine, trifluoroethanol, choline and quaternary phosphine salts. The reaction temperature ranges from room temperature to 120 °C. Most of the reported yields are excellent. Some ILs can still afford high yields even at low CO<sub>2</sub> concentration. Therefore, it is of great significance to develop new ILs for the synthesis of quinazoline-2,4(1*H*,3*H*)-diones.

2-Hydroxypyridine anion-based ILs (2-OP ILs) with two interacting sites through cooperative interactions showed high CO<sub>2</sub> absorption capacity in previous results.<sup>14</sup> Theoretically, a high CO<sub>2</sub> absorption capacity indicates a high extent of CO<sub>2</sub> activation, followed by a low energy barrier for CO<sub>2</sub> conversion. It is reported that the 2-OP ILs can be efficient for catalyzing the cycloaddition of CO<sub>2</sub> with epoxides under mild conditions.<sup>15</sup> We wonder whether these 2-OP ILs could catalyze the CO<sub>2</sub> transformation in the synthesis of quinazoline-2,4(1*H*,3*H*)-diones. Therefore, a series of 2-OP ILs as illustrated in **Figure 2** was applied in catalyzing the reaction of CO<sub>2</sub> and 2-aminobenzonitrile. These 2-OP ILs were found to be effective for this reaction in the absence of any other solvents and cocatalysts at atmospheric pressure.



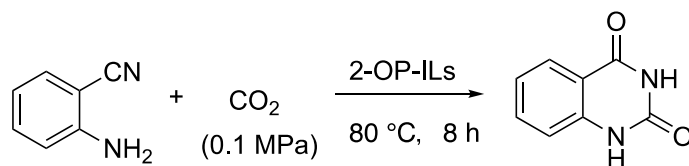
**Figure 1.** Structures and reaction conditions of reported ILs for transformation of CO<sub>2</sub> into quinazoline-2,4(1*H*,3*H*)-diones at atmospheric pressure



**Figure 2.** 2-OP ILs used in this work

At first the types of 2-OP ILs were screened, and the results are shown in **Table 1**. Previous research has shown that catalytic activity is dependent on the basicity of the IL anion, as well as the cation contributes toward the required physical properties of the ILs.<sup>6</sup> So, five representative cations were chosen to synthesis 2-OP ILs in this work. It was found that 2-OP IL with choline as cation was the best, followed by DBU, tetramethylguanidine and tetrabutylammonium hydroxide, while the ionic liquid with tetramethylammonium cation was the worst. Combined with the literature reports,<sup>6</sup> it is speculated that in addition to the strong alkalinity of choline cation, the hydroxy groups in choline molecules could also catalyze and activate the reaction.

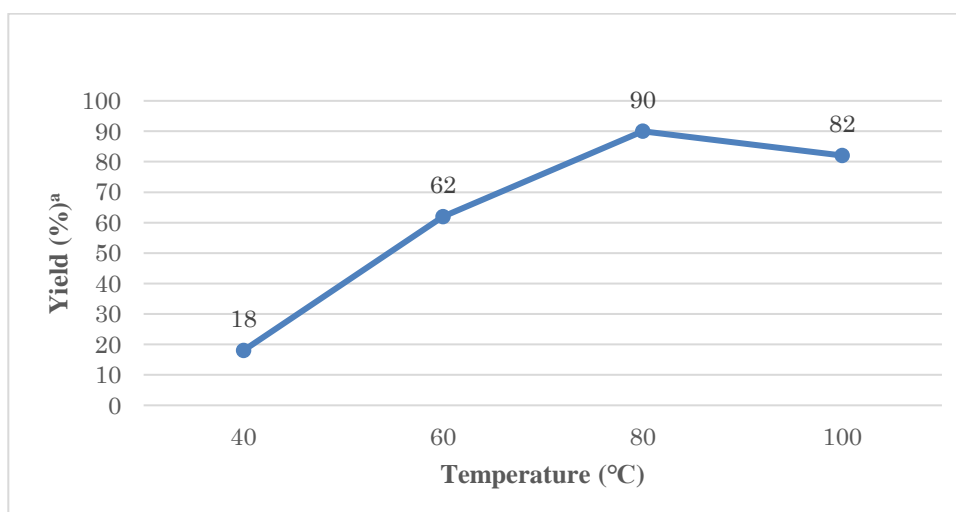
After obtaining the optimized ionic liquid [Ch][2-OP], we further optimized the reaction conditions, and the results are shown in **Figure 3**. The first step was to optimize the reaction temperature. Raising the temperature helped to accelerate the reaction, while also reducing the viscosity of the ionic liquid and promoting the dissolution of the product. When the temperature was at 80 °C, the reaction achieved the best yield. When it increased to 100 °C or decreased to 60 °C, the yield decreased. It is noteworthy that the reaction system gradually solidified as the reaction progressed when the temperature decreased to 40 °C, causing the reaction to be unable to proceed further. Next is the optimization of reaction time. We found that the reaction could achieve a moderate yield in 1 h. However, increasing the time did not result in a significant increase in yield until the highest yield was reached at 9 h. Further prolonging the time resulted in a decrease in yield. Finally, the raw material ratio was optimized. When the mole ratio of 2-aminobenzonitrile and [Ch][2-OP] was changed to 1:1, the yield was reduced to 76%. Summarily, the optimal reaction conditions were as follows: 3 equiv. [Ch][2-OP], 0.1 MPa CO<sub>2</sub>, 80 °C for 9 h.

**Table 1.** Catalyst screening of different 2-OP ILs

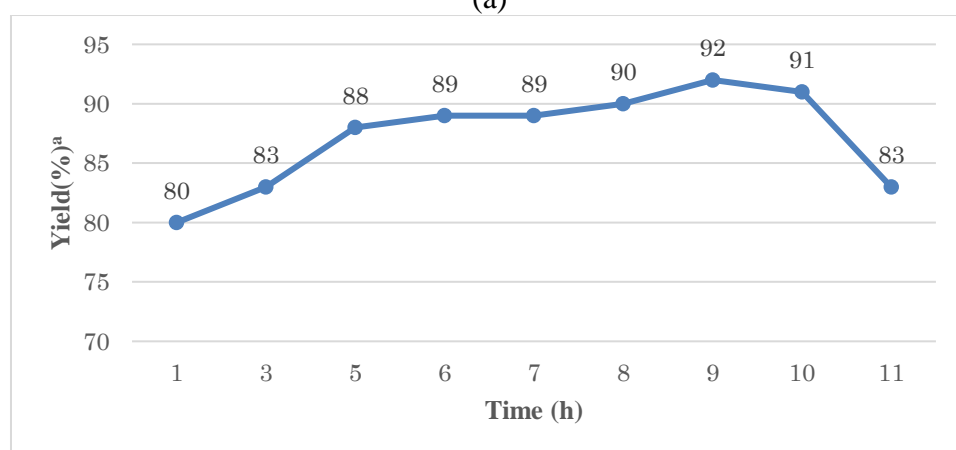
Entry <sup>a</sup>	2-OP-ILs	Yield(%) <sup>b</sup>
1	[HDBU][2-OP]	78
2	[N <sub>1111</sub> ][2-OP]	63
3	[N <sub>4444</sub> ][2-OP]	76
4	[Ch][2-OP]	90
5	[HTMG][2-OP]	73

<sup>a</sup> Reaction conditions: 2-aminobenzonitrile (1.0 mmol), CO<sub>2</sub> (0.1 MPa), 8 h, IL amount (3 mmol)

<sup>b</sup> Isolated yield



(a)



(b)

**Figure 3.** Effects of different reaction parameters on the product yield, (a) temperature, (b) reaction time.

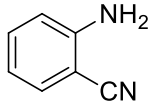
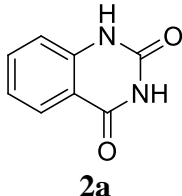
Standard conditions: 2-aminobenzonitrile (1.0 mmol), CO<sub>2</sub> (0.1 MPa), 8 h, [Ch][2-OP] amount (3.0 mmol)

<sup>a</sup> Isolated yield

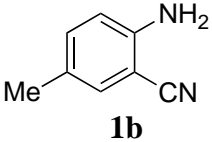
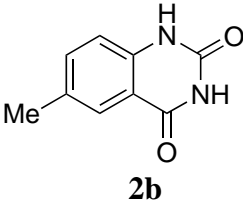
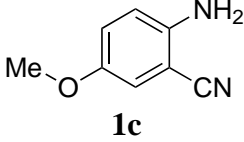
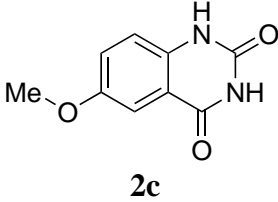
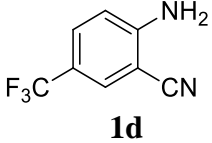
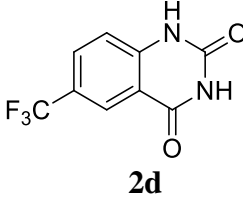
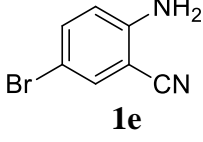
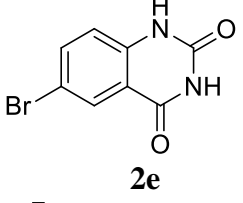
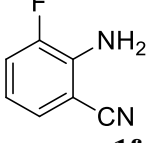
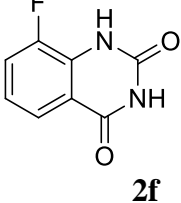
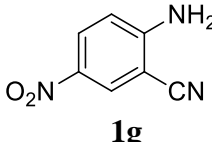
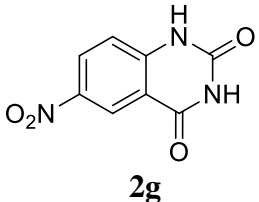
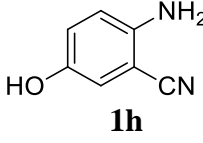
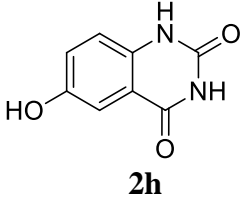
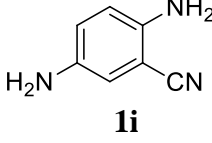
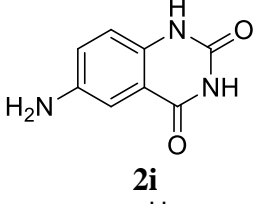
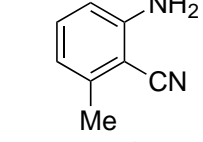
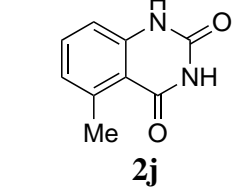
We conducted a study on the adaptability of the substrate under optimized reaction conditions, and the results are shown in **Table 2**. The results show that [Ch][2-OP] has a good catalytic conversion effect on 4-substituted 2-aminobenzonitrile with electron withdrawing or electron donating groups. Among which the yield of the substrates substituted with 4-methoxy and 4-methyl are the highest. However, the yield of nitro substituted compounds is relatively low, and the crude product undergoes column chromatography to obtain a yellow solid with a yield of 50%. These results indicate that substrates replaced by strong electron withdrawing groups have lower yields, possibly due to the electron withdrawing groups causing a decrease in the alkalinity of the amino groups on the benzene ring and a decrease in their ability to bind to CO<sub>2</sub>. The situation where the substrates were 2-amino-5-hydroxybenzonitrile and 2,5-diaminobenzonitrile was also studied, and it was found that 4-amino group and 4-hydroxy group had no significant impact on the reaction. Corresponding products can be obtained without prior group protection. Finally, we conducted a study on the 3-substituted substrates and found that the reaction yield was significantly reduced. Especially for substrate substituted with 3-trifluoromethyl, we were unable to obtain corresponding products under this reaction condition. The speculated reason was that the steric hindrance of the 3-substituted group had a negative impact on the intramolecular rearrangement.

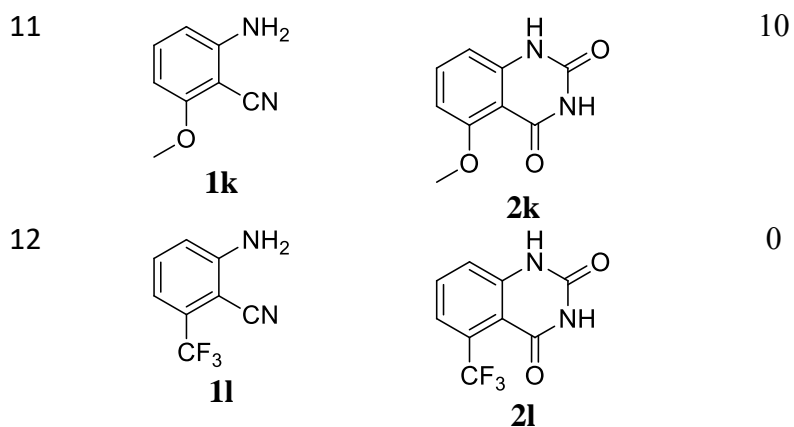
To gain more information about the effect of [Ch][2-OP], the CO<sub>2</sub> absorption experiment was conducted. As shown in **Scheme 1**, [Ch][2-OP] can capture 0.89 mol CO<sub>2</sub> per mol IL at 30 °C in 60 minutes due to its basicity. We speculate that a single carbon dioxide complex may have been generated. Then we conducted <sup>13</sup>C NMR spectral analysis on this complex and [Ch][2-OP], and their stacked spectra is shown in **Figure 4**. From this spectrum, the cationic part ([Ch]) of the ionic liquid remains unchanged, while the anionic part undergoes significant changes due to the absorption of CO<sub>2</sub>. A clear peak of carbonyl carbon appears at 160.62 ppm, which is consistent with the literature report.<sup>9</sup> Finally, this [Ch][2-OP]-CO<sub>2</sub> complex was used to the synthesis of quinazoline-2,4-(1*H*,3*H*)-dione and 87% yield of product was got when there was no more CO<sub>2</sub> introduced. It may be ascribed to the moderate interaction between [2-OP] and CO<sub>2</sub>, and 2-aminobenzonitrile is easy to acquire CO<sub>2</sub> from [Ch][2-OP]-CO<sub>2</sub> complex, indicating that this complex is the actual catalyst in the reaction.

**Table 2.** Synthesis of various quinazoline-2,4-(1*H*,3*H*)-diones

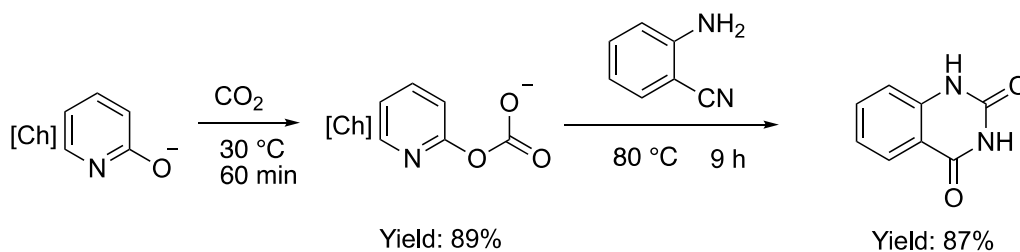
Entry <sup>a</sup>	Substrate	Product	Yield (%) <sup>b</sup>
1	 <b>1a</b>	 <b>2a</b>	92

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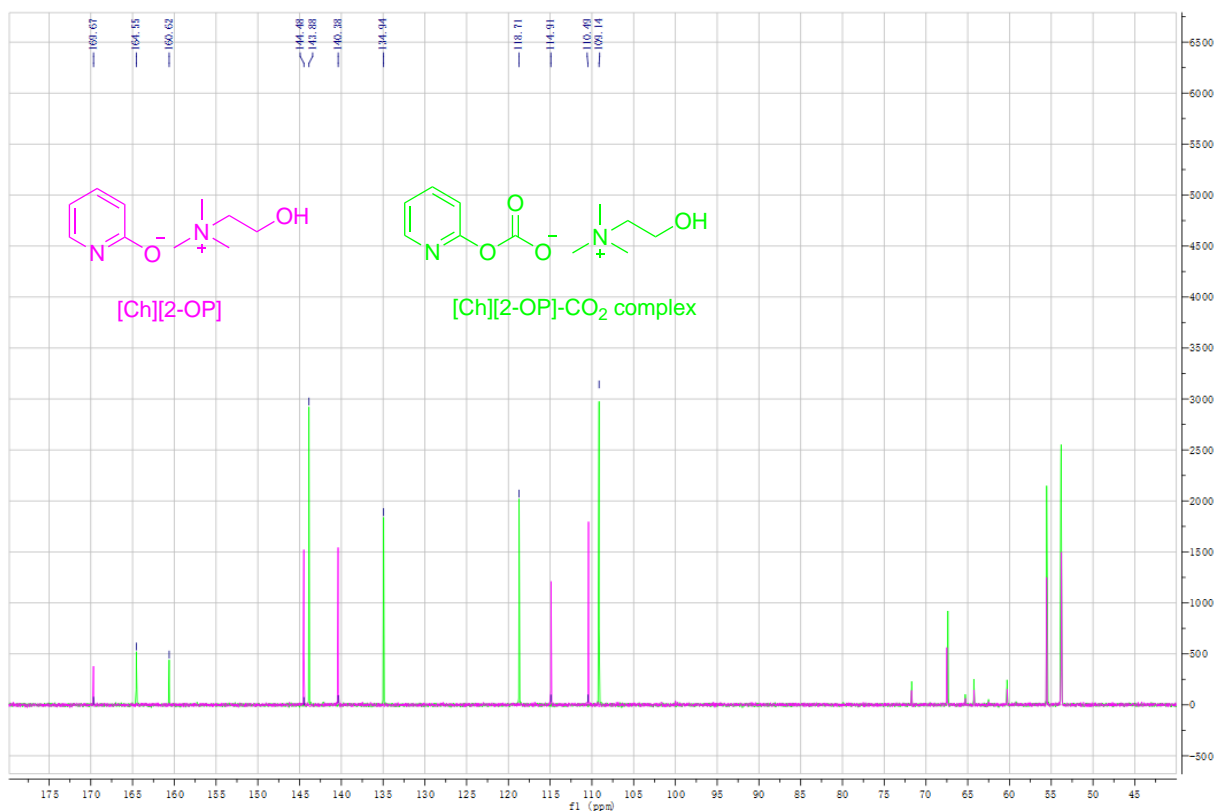
2	 <b>1b</b>	 <b>2b</b>	95
3	 <b>1c</b>	 <b>2c</b>	95
4	 <b>1d</b>	 <b>2d</b>	85
5	 <b>1e</b>	 <b>2e</b>	88
6	 <b>1f</b>	 <b>2f</b>	90
7 <sup>c</sup>	 <b>1g</b>	 <b>2g</b>	50
8	 <b>1h</b>	 <b>2h</b>	82
9	 <b>1i</b>	 <b>2i</b>	93
10	 <b>1j</b>	 <b>2j</b>	14



<sup>a</sup> Reaction conditions: 2-aminobenzonitrile (1.0 mmol), CO<sub>2</sub> (0.1 MPa), 9 h, [Ch][2-OP] amount (3 equiv.). <sup>b</sup> Isolated yield. <sup>c</sup> 6 mmol of [Ch][2-OP] was used. The crude product was purified by column chromatography (eluent: Petroleum ether/ EtOAc = 1:1)



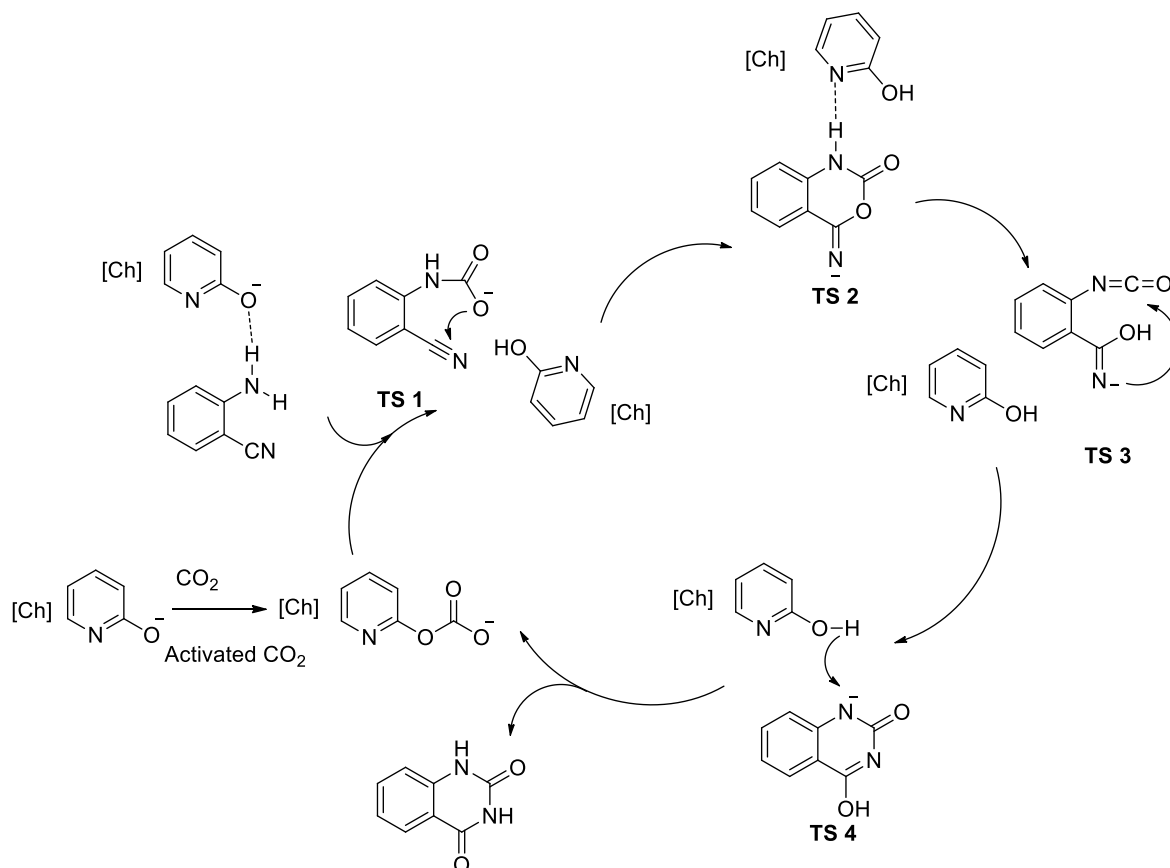
**Scheme 1.** The CO<sub>2</sub> absorption experiment of [Ch][2-OP]



**Figure 4.** The stacked <sup>13</sup>C NMR spectra of [Ch][2-OP] (purple) and [Ch][2-OP]-CO<sub>2</sub> complex (green)

According to literature reports<sup>6,14</sup> and our NMR results, we propose a possible reaction mechanism, as shown in **Scheme 2**. Firstly, the ionic liquid absorbs CO<sub>2</sub> to form [Ch][2-OP]-CO<sub>2</sub> complex. At the same time, the basic anion in the ionic liquid can also activate the amino group on the 2-aminobenzonitrile to transfer the activated carbon dioxide to form the intermediate **TS 1**. The carboxyl oxygen anion molecule of this intermediate undergoes nucleophilic attack on the cyanide group, generating intermediate **TS 2**. Under alkaline conditions, the intermediate **TS 3** of isocyanate is generated through intramolecular rearrangement, and then the intermediate **TS 4** is generated through intramolecular reaction. The intermediate **TS 4** was unstable, and the final product, quinazoline-2,4(1*H*,3*H*)-dione, is obtained by isomerization.

In conclusion, a series of 2-OP ILs was synthesized and successfully applied to the synthesis of quinazoline-2,4(1*H*,3*H*)-diones. The preferred ionic liquid [Ch][2-OP] can catalyze the cyclization of a variety of 4-substituted 2-aminobenzonitriles and CO<sub>2</sub> under atmospheric pressure, and the corresponding quinazoline-2,4(1*H*,3*H*)-diones can achieve moderate to excellent yields. However, the synthetic scheme is not very effective for 3-substituted 2-aminobenzonitriles, possibly due to steric hindrance. The CO<sub>2</sub> absorption experiment and <sup>13</sup>C NMR analysis show that [Ch][2-OP]-CO<sub>2</sub> complex is the real catalyst for this reaction. This method is simple in operation and does not require the use of additional organic solvents and metal catalysts, providing a new pathway for the conversion and utilization of CO<sub>2</sub>.



**Scheme 2.** Possible reaction mechanism



## EXPERIMENTAL

All reagents, including substituted 2-aminobenzonitriles, 2-hydroxyethyltrimethylammonium hydroxide (44 wt.% in water), 1,8-diazabicyclo[5.4.0]undec-7-ene, tetramethylammonium hydroxide (25% w/w in water), tetrabutylammonium hydroxide (50 wt.% in water), and tetramethylguanidine were purchased from Energy Chemistry Co. Ltd or Shanghai Aladdin Biochemical Technology Co. Ltd. They were used directly without further purification. CO<sub>2</sub> and Ar was purchased from Hangzhou Jingong Special Gas Co. Ltd. <sup>1</sup>H NMR and <sup>13</sup>C NMR studies were carried out with a Bruker AVANCE III 500 (500 MHz, 125 MHz) spectrometer or Bruker AVANCE III HD 600 (600 MHz, 150 MHz) with D<sub>2</sub>O or DMSO-*d*<sub>6</sub> as the solvent. High resolution mass spectrometry (HRMS) data for some compounds were recorded on a Waters Xevo G2-XS QTof.

**The Preparation of 2-OP ILs.** According to the reported procedures,<sup>9,15</sup> the protic ILs were synthesized via the neutralization of corresponding base and 2-hydroxypyridine respectively. In a typical process, equimolar 2-hydroxypyridine (50 mmol) was added to a 100 mL EtOH solution of 2-hydroxyethyltrimethylammonium hydroxide (50 mmol), then the mixture was stirred at room temperature for 10 h under He atmosphere. The product [Ch][2-OP] was obtained as orange transparent viscous liquid in quantitative yield after solvent removal by vacuum distillation with a rotary evaporator, then stored over 4 Å molecular sieves before use. Other protic ILs were prepared similarly. The structures of them were confirmed by NMR.

[Ch][2-OP], orange viscous liquid, <sup>1</sup>H NMR (600 MHz, D<sub>2</sub>O) δ 7.65 (dd, 1H, <sup>4</sup>J = 1.8 Hz, J = 5.4 Hz, Ar-H), 7.39-7.35 (m, 1H, Ar-H), 6.41-6.37 (m, 1H, Ar-H), 6.31 (d, 1H, J = 8.4 Hz, Ar-H), 3.87-3.83 (m, 2H, CH<sub>2</sub>), 3.26 (t, 2H, J = 5.2 Hz, CH<sub>2</sub>), 2.97 (s, 9H, CH<sub>3</sub>). <sup>13</sup>C NMR (150 MHz, D<sub>2</sub>O) δ 169.68, 144.49, 140.39, 114.88, 110.41, 67.50, 55.55, 53.80, 53.78, 53.75.

[HDBU][2-OP], orange transparent liquid, <sup>1</sup>H NMR (500 MHz, D<sub>2</sub>O) δ 7.64 (dd, 1H, <sup>4</sup>J = 2.0 Hz, J = 5.4 Hz, Ar-H), 7.44-7.40 (m, 1H, Ar-H), 6.44-6.41 (m, 1H, Ar-H), 6.34 (d, 1H, J = 7.5 Hz, Ar-H), 3.42-3.41 (m, 2H, CH<sub>2</sub>), 3.34 (t, 2H, CH<sub>2</sub>), 3.17 (t, 2H, CH<sub>2</sub>), 2.48-2.46 (m, 2H, CH<sub>2</sub>), 1.89-1.84 (m, 2H, CH<sub>2</sub>), 1.61-1.54 (m, 6H, CH<sub>2</sub>).

[N<sub>1111</sub>][2-OP], colorless viscous liquid, <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>) δ 7.65 (dd, 1H, <sup>4</sup>J = 2.5 Hz, J = 5.0 Hz, Ar-H), 6.91-6.88 (m, 1H, Ar-H), 5.78-5.74 (m, 2H, Ar-H), 3.14 (s, 12H, CH<sub>3</sub>).

[N<sub>4444</sub>][2-OP], colorless viscous liquid, <sup>1</sup>H NMR (500 MHz, D<sub>2</sub>O) δ 7.67 (dd, 1H, <sup>4</sup>J = 1.8 Hz, J = 5.0 Hz, Ar-H), 7.58-7.55 (m, 1H, Ar-H), 6.53 (t, 1H, J = 5.2 Hz, Ar-H), 6.49 (d, 1H, J = 8.5 Hz, Ar-H), 3.19-3.15 (m, 8H, CH<sub>2</sub>), 1.65-1.59 (m, 8H, CH<sub>2</sub>), 1.37-1.30 (m, 8H, CH<sub>2</sub>), 0.92 (t, 12H, CH<sub>3</sub>).

[HTMG][2-OP], colorless viscous liquid,  $^1\text{H}$  NMR (500 MHz,  $\text{D}_2\text{O}$ )  $\delta$  7.59 (dd, 1H,  $^4J = 1.8$  Hz,  $J = 5.8$  Hz, Ar-H), 7.50-7.47 (m, 1H, Ar-H), 6.46-6.43 (m, 1H, Ar-H), 6.40 (d, 1H,  $J = 9.0$  Hz, Ar-H), 2.83 (s, 12H,  $\text{CH}_3$ ).

**General Procedure for the Synthesis of Quinazoline-2,4-(1H,3H)-diones.** 2-Aminobenzonitrile (1 mmol) and [Ch][2-OP] (3 mmol) were added into a Schlenk flask, connecting with a  $\text{CO}_2$  balloon. Then reaction mixture was stirred for desired time at  $80^\circ\text{C}$ . After cooling to room temperature, 10 mL water was added into the reactor. The obtained solution was adjusted to pH 6-7 with 1 mol/L hydrochloric acid, and then white solid precipitated. After filtration, the precipitate was washed with water and EtOAc. The obtained solid was dried and directly used for NMR analysis for structural identification. The physical data of **2a-b** and **2e** were identical with those reported in literatures.<sup>6,11</sup> Compounds **2c-d** and **2f-k** were confirmed by NMR and HRMS.

Quinazoline-2,4(1H,3H)-dione (**2a**), white solid, yield 92%, mp  $>300^\circ\text{C}$ ,  $^1\text{H}$  NMR (600 MHz,  $\text{DMSO}-d_6$ )  $\delta$  11.28 (s, 1H, NH), 11.14 (s, 1H, NH), 7.89 (d, 1H,  $J = 7.8$  Hz, Ar-H), 7.64 (t, 1H,  $J = 8.1$  Hz, Ar-H), 7.19-7.16 (m, 2H, Ar-H).  $^{13}\text{C}$  NMR (150 MHz,  $\text{DMSO}-d_6$ )  $\delta$  163.30, 150.76, 141.34, 135.43, 127.42, 122.79, 115.78, 114.81.

6-Methylquinazoline-2,4(1H,3H)-dione (**2b**), white solid, yield 95%, mp  $>300^\circ\text{C}$ ,  $^1\text{H}$  NMR (500 MHz,  $\text{DMSO}-d_6$ )  $\delta$  11.13 (br s, 2H, NH), 7.69 (s, 1H, Ar-H), 7.46 (dd, 1H,  $^4J = 2.0$  Hz,  $J = 8.3$  Hz, Ar-H), 7.07 (d, 1H,  $J = 8.0$  Hz, Ar-H), 2.32 (s, 3H,  $\text{CH}_3$ ).  $^{13}\text{C}$  NMR (125 MHz,  $\text{DMSO}-d_6$ )  $\delta$  162.78, 150.24, 138.65, 135.89, 131.47, 126.41, 115.22, 114.11, 20.16.

6-Methoxyquinazoline-2,4(1H,3H)-dione (**2c**), white solid, yield 95%, mp  $>300^\circ\text{C}$ ,  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO}-d_6$ )  $\delta$  11.25 (s, H, NH), 11.02 (s, H, NH), 7.33 (d, 1H,  $^4J = 2.4$  Hz, Ar-H), 7.28 (dd, 1H,  $^4J = 2.2$  Hz,  $J = 7.0$  Hz, Ar-H), 7.12 (d, 1H,  $J = 7.2$  Hz, Ar-H), 3.79 (s, 3H,  $\text{CH}_3$ ).  $^{13}\text{C}$  NMR (100 MHz,  $\text{DMSO}-d_6$ )  $\delta$  162.67, 154.55, 150.02, 134.93, 123.78, 116.88, 114.79, 107.96, 55.49. HRMS (ESI)  $[\text{M}+\text{H}]^+$  calculated for  $\text{C}_9\text{H}_9\text{N}_2\text{O}_3$ : 193.0613, found: 193.0591.

6-Trifluoromethylquinazoline-2,4(1H,3H)-dione (**2d**), white solid, yield 85%, mp  $>300^\circ\text{C}$ ,  $^1\text{H}$  NMR (500 MHz,  $\text{DMSO}-d_6$ )  $\delta$  11.55 (s, 2H, NH), 8.11 (s, 1H, Ar-H), 7.97 (d, 1H,  $J = 8.5$  Hz, Ar-H), 7.35 (d, 1H,  $J = 8.5$  Hz, Ar-H),  $^{13}\text{C}$  NMR (125 MHz,  $\text{DMSO}-d_6$ )  $\delta$  161.96, 150.14, 143.79, 131.19 (d,  $J_{\text{C-F}} = 6.38$  Hz), 124.14 (q,  $J_{\text{C-F}} = 7.88$  Hz), 123.87 (q,  $J_{\text{C-F}} = 540$  Hz), 122.53 (q,  $J_{\text{C-F}} = 65$  Hz), 116.61, 114.44. HRMS (ESI)  $[\text{M}-\text{H}]^-$  calculated for  $\text{C}_9\text{H}_4\text{F}_3\text{N}_2\text{O}_2$ : 229.0225, found: 229.0219.

6-Bromoquinazoline-2,4(1H,3H)-dione (**2e**), white solid, yield 88%, mp  $>300^\circ\text{C}$ ,  $^1\text{H}$  NMR (500 MHz,  $\text{DMSO}-d_6$ )  $\delta$  11.37 (s, 2H, NH), 7.94 (d, 1H,  $^4J = 2.0$  Hz, Ar-H), 7.97 (dd, 1H,  $^4J = 2.3$  Hz,  $J = 8.8$  Hz, Ar-H), 7.35 (d, 1H,  $J = 8.5$  Hz, Ar-H).  $^{13}\text{C}$  NMR (125 MHz,  $\text{DMSO}-d_6$ )  $\delta$  161.69, 150.01, 140.04, 137.44, 128.87, 117.73, 116.16, 113.78.

8-Fluoroquinazoline-2,4(1H,3H)-dione (**2f**), white solid, yield 90%, mp  $>250^\circ\text{C}$  (decomposition),  $^1\text{H}$  NMR

(500 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  11.44 (s, 1H, NH), 11.29 (s, 1H, NH), 7.72 (d, 1H,  $J = 7.5$  Hz, Ar-H), 7.59-7.55 (m, 1H, Ar-H), 7.19-7.15 (m, 1H, Ar-H). HRMS (ESI)  $[M+H]^+$  calculated for C<sub>8</sub>H<sub>6</sub>FN<sub>2</sub>O<sub>2</sub>: 181.0413, found: 181.0396.

6-Nitroquinazoline-2,4(1*H*,3*H*)-dione (**2g**), yellow solid, yield 50%, mp >300 °C, <sup>1</sup>H NMR (600 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  11.77 (s, 1H, NH), 11.72 (s, 1H, NH), 8.59 (d, 1H, <sup>4</sup> $J = 2.4$  Hz, Ar-H), 8.46 (dd, 1H, <sup>4</sup> $J = 2.4$  Hz,  $J = 9.0$  Hz, Ar-H), 7.32 (d, 1H,  $J = 9.0$  Hz, Ar-H). <sup>13</sup>C NMR (150 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  162.12, 150.47, 146.14, 142.34, 130.09, 123.59, 117.16, 115.03. HRMS (ESI)  $[M-H]^-$  calculated for C<sub>8</sub>H<sub>4</sub>N<sub>3</sub>O<sub>4</sub>: 206.0202, found: 206.0201.

6-Hydroxyquinazoline-2,4(1*H*,3*H*)-dione (**2h**), brown solid, yield 82%, mp >300 °C, <sup>1</sup>H NMR (600 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  11.15 (s, 1H, NH), 10.89 (s, 1H, NH), 9.60 (s, 1H, OH), 7.22 (d, 1H, <sup>4</sup> $J = 2.4$  Hz, Ar-H), 7.10 (dd, 1H, <sup>4</sup> $J = 2.7$  Hz,  $J = 8.7$  Hz, Ar-H), 7.03 (d, 1H,  $J = 9.0$  Hz, Ar-H). <sup>13</sup>C NMR (150 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  163.21, 153.08, 150.51, 134.02, 124.17, 117.13, 115.51, 111.15. HRMS (ESI)  $[M+H]^+$  calculated for C<sub>8</sub>H<sub>7</sub>N<sub>2</sub>O<sub>3</sub>: 179.0457, found: 179.0441.

6-Aminoquinazoline-2,4(1*H*,3*H*)-dione (**2i**), yellow solid, yield 93%, mp >300 °C, <sup>1</sup>H NMR (600 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  10.99 (s, 1H, NH), 10.72 (s, 1H, NH), 7.06 (d, 1H, <sup>4</sup> $J = 2.4$  Hz, Ar-H), 6.93-6.89 (m, 2H, Ar-H), 5.16 (s, 2H, NH<sub>2</sub>). <sup>13</sup>C NMR (150 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  163.48, 150.44, 144.65, 131.81, 122.96, 116.46, 115.44, 109.44. HRMS (ESI)  $[M+H]^+$  calculated for C<sub>8</sub>H<sub>8</sub>N<sub>3</sub>O<sub>2</sub>: 178.0617, found: 178.0596.

5-Methylquinazoline-2,4(1*H*,3*H*)-dione (**2j**), orange solid, yield 14%, mp >300 °C, <sup>1</sup>H NMR (600 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  11.05 (s, 1H, NH), 11.00 (s, 1H, NH), 7.45 (t, 1H,  $J = 7.8$  Hz, Ar-H), 7.01 (d, 1H,  $J = 7.8$  Hz, Ar-H), 6.94 (d, 1H,  $J = 7.2$  Hz, Ar-H), 2.65 (s, 3H, CH<sub>3</sub>). <sup>13</sup>C NMR (150 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  164.10, 150.52, 142.64, 141.44, 134.24, 125.64, 113.93, 112.96, 22.54. HRMS (ESI)  $[M+H]^+$  calculated for C<sub>9</sub>H<sub>9</sub>N<sub>2</sub>O<sub>2</sub>: 177.0664, found: 177.0658.

5-Methoxyquinazoline-2,4(1*H*,3*H*)-dione (**2k**), yellow solid, yield 10%, mp >300 °C, <sup>1</sup>H NMR (600 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  10.97 (s, 1H, NH), 10.87 (s, 1H, NH), 7.51 (t, 1H,  $J = 8.1$  Hz, Ar-H), 6.72-6.70 (m, 2H, Ar-H), 3.81 (s, 3H, OCH<sub>3</sub>). <sup>13</sup>C NMR (150 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  161.31, 160.94, 150.59, 143.57, 135.83, 107.74, 105.38, 104.21, 56.32. HRMS (ESI)  $[M+H]^+$  calculated for C<sub>9</sub>H<sub>9</sub>N<sub>2</sub>O<sub>3</sub>: 193.0613, found: 193.0591.

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