

## Green and efficient synthesis of new pyrido[2,3-*d*]pyrimidine derivatives using Pd/SBA-15 as a nanocatalyst

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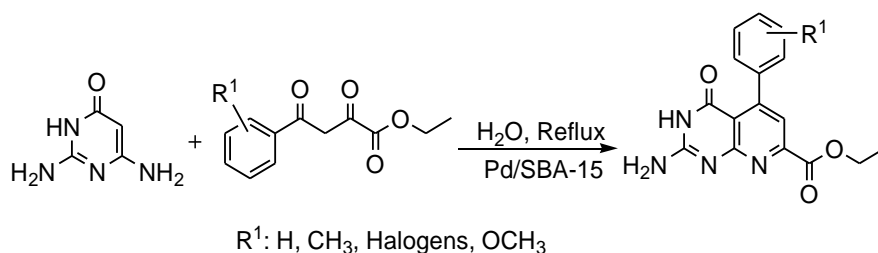
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### Abstract

N-Fused heterocycles have received significant attention over the years as valuable compounds due to their biological and pharmaceutical activities. Heterogeneous catalysts such as periodic mesoporous materials have played an important role in the synthesis of these compounds due to their outstanding properties, including nanometric pore sizes, structural homogeneity, relatively simple preparation, and ease of modification. In this study, a new and facile synthesis of pyrido[2,3-*d*]pyrimidine analogues via the condensation reactions of 2,6-diaminopyrimidin-4(3*H*)-one and ethyl-2,4-dioxo-4-phenylbutanoates in the presence of an environmentally friendly and heterogeneous catalyst, Pd/SBA-15, in water is reported. The target compounds were obtained in good to excellent isolated yields.



**Keywords:** Pyrido[2,3-*d*]pyrimidine, green synthesis, nanocatalyst, mesoporous silica, SBA-15, Pd/SBA-15, environmentally friendly



## Introduction

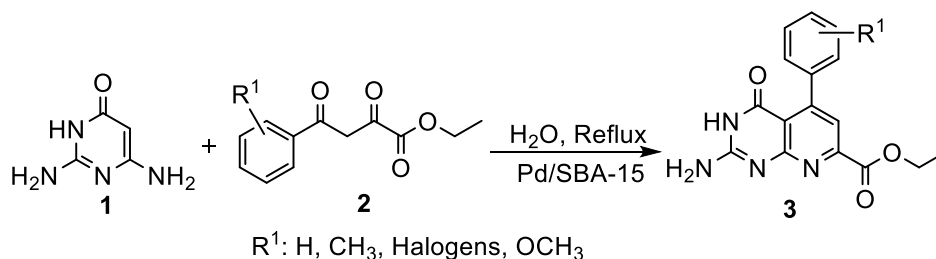
In recent years, organic synthesis has been focused towards the development of green and more eco-friendly procedures using non-toxic, non-hazardous, and environmentally friendly solvents. In this respect, several organic reactions have been performed in water which is green, readily available, inexpensive, and safe.<sup>1</sup>

N-Fused heterocycles are the main category of organic compounds which have received significant attention over the past years.<sup>2</sup> Pyrimidine-fused derivatives such as pyrido[2,3-*d*]pyrimidines are valuable compounds due to their various biological and pharmaceutical activities. They have demonstrated antitumour,<sup>3</sup> anti-inflammatory,<sup>4</sup> antibacterial,<sup>5</sup> antifungal,<sup>6</sup> and antihypertensive properties.<sup>7</sup> Also, 5-deaza isostere-4,7-diamino-*N*-(2-morpholinoethyl)-2-phenylpyrido[2,3-*d*]pyrimidine-6-carboxamides have been described as potential diuretic agents.<sup>8</sup> Although numerous reports have been published on the syntheses of pyrido[2,3-*d*]pyrimidines, the reactions are usually limited to condensation reactions, both in solution and on solid phase, suffer from having to use toxic reagents, and result in low yields following complex work-ups.<sup>9,10</sup> Following our interest in the synthesis of nitrogen containing heterocycles,<sup>11</sup> we have prepared different pyrido[2,3-*d*]pyrimidines which can be attractive from medicinal chemists' points of view.

Today, heterogeneous catalysts play an important role in the synthesis of organic compounds.<sup>12,13</sup> Recently, significant research has been devoted to the development of periodic mesoporous materials due to their outstanding properties such as nanometric pore sizes, structural homogeneity, relatively simple preparation, and ease of modification.<sup>14,15</sup> In this regard, different mesoporous silica materials including MCM-41, MCM-48, and SBA-15 have garnered lots of attention. In particular, SBA-15 has shown more efficient properties in catalysis, drug delivery systems, environmental remediation, excellent stability, and proton conductivity.<sup>16</sup> Since mesoporous silicates have larger surface areas, uniform pore structure and inert environment for inactivation of transition metal nanoparticles, it has become a notable carrier for many functional materials.<sup>17</sup>

In this respect, SBA-15-supported Pd-catalysts have emerged as a new class of nano catalysts for the synthesis of organic compounds.<sup>18</sup> Palladium ion is one of the most important metal ions which can be successfully supported on SBA-15 through various binding schemes such as ionic liquids,<sup>19</sup> PEG coating,<sup>20</sup> mercaptopropyl trimethoxy silane,<sup>21</sup> and phosphorous/nitrogen donor ligands.<sup>22</sup> In this context, we prepared SBA-15 material by the reaction of SBA-15 and a Pd/SBA-15.<sup>23</sup>

In continuation of our research program for the preparation of novel heterocyclic compounds, we have developed a highly efficient procedure for the synthesis of pyrido[2,3-*d*]pyrimidines (**3**) via the condensation reactions of 2,6-diaminopyrimidin-4(3*H*)-one (**1**) and ethyl-2,4-dioxo-4-phenylbutanoate derivatives (**2**) in the presence of an environmentally friendly and highly reactive Pd(II) complex, supported on SBA-15 as a heterogeneous catalyst, in water (Scheme 1).

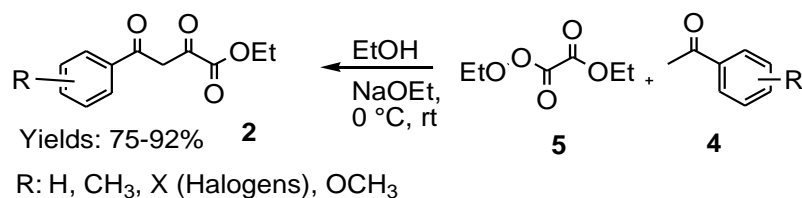


**Scheme 1.** Synthesis of novel pyrido[2,3-*d*]pyrimidines (**3**).



## Results and Discussion

Initially, the required starting materials, including 2,6-diaminopyrimidin-4(3*H*)-one (**1**) and ethyl-2,4-dioxo-4-arylbutanoates (**2**) were synthesized following the methods reported in the literature<sup>24</sup>; (**2**) was prepared from acetophenones (**4**) and diethyl oxalate (**5**) (Scheme 2).



**Scheme 2.** Synthesis of starting material (**2**) needed for the synthesis of pyrido[2,3-*d*]pyrimidine derivatives (**3**).

To obtain the most appropriate conditions for the synthesis of the desired compounds **3**, we tested the reaction of 2,6-diaminopyrimidin-4(3*H*)-one (**1**), ethyl 2,4-dioxo-4-phenylbutanoate (**2a**) and Pd/SBA-15 as a simple model substrate in various conditions (Table 1).

**Table 1.** Solvent screening for the synthesis of compound **3a**

Entry	Solvent	Temperature	Time (h)	Catalyst	Yield <sup>a</sup> (%)
1	THF	68 °C	15	Pd/SBA-15(10) <sup>b</sup>	35
2	THF	68 °C	15	Pd/SBA-15(5) <sup>b</sup>	25
3	MeOH	65 °C	13	Pd/SBA-15(10) <sup>b</sup>	20
4	MeOH	65 °C	13	Pd/SBA-15 (5) <sup>b</sup>	15
5	H <sub>2</sub> O	100 °C	3	Pd/SBA-15 (10) <sup>b</sup>	90
6	H <sub>2</sub> O	100 °C	7	Pd/SBA-15 (5) <sup>b</sup>	50
7	HCl	100 °C	15	Pd/SBA-15 (10) <sup>b</sup>	30
8	HCl	100 °C	15	Pd/SBA-15 (5) <sup>b</sup>	20
9	H <sub>2</sub> O	120 °C	20	-	5
10	DMF	130 °C	12	Pd/SBA-15 (10) <sup>b</sup>	25
11	DMF	130 °C	12	Pd/SBA-15 (5) <sup>b</sup>	35

<sup>a</sup> Isolated yield.

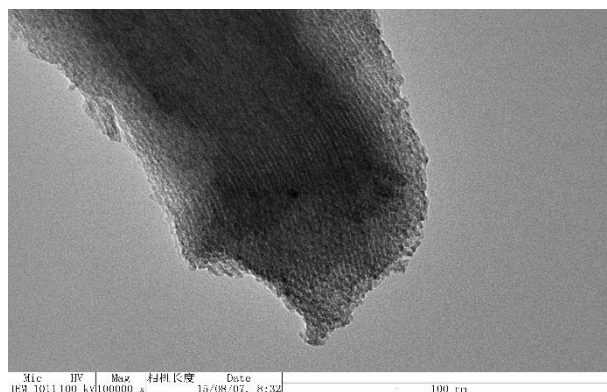
<sup>b</sup> Values in parenthesis = mol% of Pd/SBA-15.

It was found that using water in the presence of Pd/SBA-15 under reflux conditions gave the desired product in good yield (Table 1, entry 5). In the absence of Pd/SBA-15, even after a long time, only a small amount of product was formed (Table 1, entry 9). The generality of the method was then developed by the preparation of various pyrido[2,3-*d*]pyrimidines using different ethyl-2,4-dioxo-4-arylbutanoates (Table 2, entries 1-10 ).

It was observed that the desired products were obtained in good to excellent yields in almost all cases. Their structures were confirmed by IR, <sup>1</sup>H-NMR and <sup>13</sup>C-NMR spectroscopies as well as mass spectrometry.

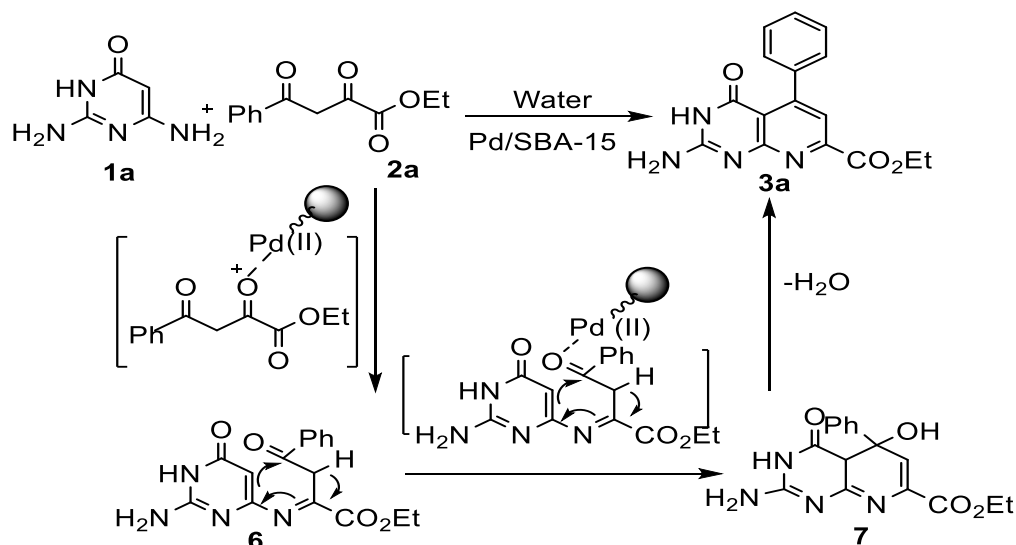


The transmission electron microscope (TEM) image of Pd/SBA-15 (Figure 1) confirmed the ordered channel structure of mesoporous materials which is retained during the complex grafting. The amount of palladium loaded on SBA/15 was determined by atomic absorption (0.14 mmol/g). Also, the hot filtrate of the reaction was examined by atomic absorption spectroscopy and no metal traces were detected.



**Figure 1.** TEM image of Pd/SBA-15.

A plausible mechanism for the formation of compound **3a** is proposed in Scheme 3. Initially, we believe the carbonyl group is activated by the Pd ion and then attacked by the  $\text{NH}_2$  group of **1** to give the intermediate **6**. Next, a cyclization reaction followed by elimination of  $\text{H}_2\text{O}$  leads to formation of product **3a**.



**Scheme 3.** Plausible mechanism for the formation of product **3a**.

Our results showed that the presence of electron withdrawing groups on the aryl ring gave the corresponding product **3** in higher yields, which can be associated with activation of carbonyl group in intermediate **6** (Table 2, entries 2-6). The presence of electron donating groups led to lower yields of products (Table 2, entries 7-12).

There are several reports for using recycled catalysts under different conditions, e.g., the synthesis of pyridopyrazine and quinoxaline derivatives with Cu/SBA-15,<sup>13</sup> and the reduction of 4-nitrophenol and 2-nitroaniline with silver nanoparticles. In all of these reactions, the catalyst is recycled.<sup>25</sup> To test the lifetime



and reusability of the heterogeneous system, a series of experiments were conducted for the model reaction under optimized conditions. After completion of the first reaction with 85% yield, the catalyst was recovered by filtration, washed with ethanol and dried at 80 °C for 60 min. The recovered catalyst was employed in another reaction run. There is one run in this reaction.

**Table 2.** Synthesis of pyrido[2,3-*d*]pyrimidine derivatives (3)

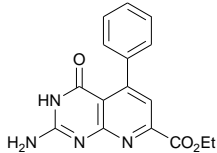
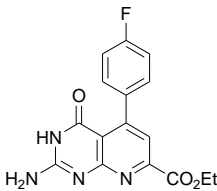
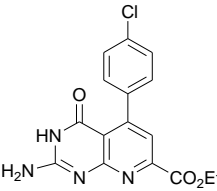
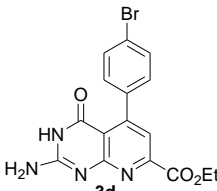
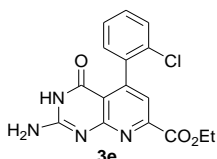
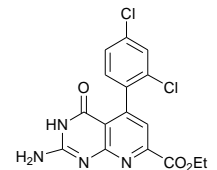
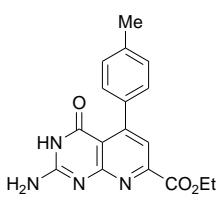
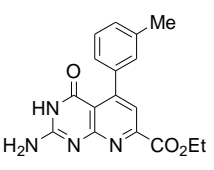
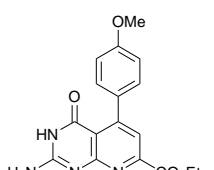
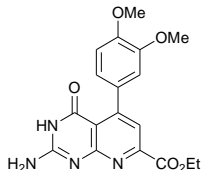
Entry	R <sup>1</sup>	Product	Yield (%) <sup>a</sup>
1	H	 3a	84
2	4-F	 3b	85
3	4-Cl	 3c	82
4	4-Br	 3d	86
5	2-Cl	 3e	84
6	2,4-(Cl) <sub>2</sub>	 3f	81
7	4-Me	 3g	80



Table 2. Continued

Entry	R <sup>1</sup>	Product	Yield (%) <sup>a</sup>
8	3-Me	 3h	75
9	4-OMe	 3i	75
10	3,4-(OMe) <sub>2</sub>	 3j	73

<sup>a</sup> Isolated yield

## Conclusions

We report a simple and efficient route for the synthesis of new pyrido[2,3-*d*]pyrimidines using readily available starting materials. Several benefits, including the use of water as a (green) solvent, operational simplicity, easy work-up procedure including no requirement of time-consuming purification steps, and high yields of the products, make it a suitable method for the syntheses of the title compounds.

## Experimental Section

**General.** Melting points were measured on a Kofler hot-stage apparatus and are uncorrected. <sup>1</sup>H- and <sup>13</sup>C-NMR spectra were recorded on a Bruker FT-500 using TMS as an internal standard. The abbreviations used are: s, singlet; d, doublet and m, multiplet. IR spectra were recorded on a Nicolet Magna FTIR 550 spectrophotometer (KBr disks). MS were recorded with an Agilent Technology (HP) mass spectrometer operating at an ionization potential of 70 eV. Elemental analysis was conducted using an Elementar Analysensysteme GmbH VarioEL in CHNS mode. The Pd/SBA-15 catalyst was characterized by different techniques including transmission electron microscopy (TEM) and scanning electron microscopy (SEM). The concentration of Pd (II) in immobilized SBA-15 was determined by atomic absorption (AA) spectroscopy. For this purpose, 0.1 g of the catalyst was digested using HNO<sub>3</sub> and stirred at room temperature for a week. The mixture was then filtered, and the solid washed several times with water. The total concentration of the Pd(II) ions on SBA/15 was 0.14 mmol/g.



**General procedure for the synthesis of oxopyrido[2,3-*d*]pyrimidine derivatives (3).** In a round-bottomed flask equipped with a magnet and a condenser, 6-diaminopyrimidin-4(3*H*)-one 1 (1 mmol), ethyl 2,4-dioxo-4-arylbutanoates 2 (1 mmol), and Pd/SBA-15 (10 mol%) were added to water (10 mL) at room temperature. The mixture was refluxed for 3 h, and the progress of the reaction was monitored by TLC (ethyl acetate/*n*-hexane: 1/2). After completion of the reaction, the catalyst was filtered from the hot mixture, the filtrate was left to cool, and the precipitate was filtered off and purified by recrystallization from the same mixture concentration of EtOH/water (1:1).

**Ethyl-2-amino-3,4-dihydro-4-oxo-5-phenylpyrido[2,3-*d*] pyrimidine-7-carboxylate (3a).** Yield: (8.2 mg, 84%); yellow crystals; mp 120-122 °C; IR (KBr): 1680, 1720, 2998, 3019, 3167, 3289 cm<sup>-1</sup>. <sup>1</sup>H NMR (500 MHz, DMSO): δ<sub>H</sub> = 1.33 (t, *J* 7 Hz, 3H, CH<sub>3</sub>), 4.36 (q, *J* 7 Hz, 2H, OCH<sub>2</sub>), 6.90 (s, 2H, NH<sub>2</sub>), 7.51-7.53 (m, 3H, Ar), 7.67 (s, 1H, pyridine), 8.17-8.19 (m, 2H, Ar). <sup>13</sup>C NMR (125 MHz, DMSO): 13.7, 60.3, 106.0, 115.4, 127.0, 129.9, 130.6, 130.9, 131.3, 137.9, 142.4, 154.9, 162.0, 167.0. Anal. Calcd for C<sub>16</sub>H<sub>14</sub>N<sub>4</sub>O<sub>3</sub>: C, 61.93; H, 4.55; N, 18.06. Found: C, 61.71; H, 4.26; N, 17.85.

**Ethyl-2-amino-5-(4-fluorophenyl)-3,4-dihydro-4-oxopyrido [2,3-*d*]pyrimidine-7-carboxylate (3b).** Yield: (9 mg, 85%); yellow crystals; mp 210 °C; IR (KBr): 1678, 1727, 3107, 3173, 3337 cm<sup>-1</sup>. <sup>1</sup>H NMR (500 MHz, DMSO): δ<sub>H</sub> = 1.31 (t, *J* 7 Hz, 3H, CH<sub>3</sub>), 4.34 (q, *J* 7 Hz, 2H, OCH<sub>2</sub>), 6.84 (s, 2H, NH<sub>2</sub>), 7.33 (t, *J* 8.5 Hz, 2H, Ar), 7.68 (s, 1H, pyridine), 8.24 (t, *J* 8.5 Hz, 2H, Ar). <sup>13</sup>C NMR (125 MHz, DMSO): 13.7, 61.3, 105.8, 111.3, 115.4, 115.8 (d, *J*<sub>C-F</sub> 22 Hz), 129.6 (d, *J*<sub>C-F</sub> 8.7 Hz), 132.7, 135.1, 142.4, 155.8, 159.6, 163.6 (d, *J*<sub>C-F</sub> 247 Hz), 167.2. Anal. Calcd for C<sub>16</sub>H<sub>13</sub>FN<sub>4</sub>O<sub>3</sub>: C, 58.54; H, 3.99; N, 17.07. Found: C, 58.31; H, 4.18; N, 17.31.

**Ethyl-2-amino-5-(4-chlorophenyl)-3,4-dihydro-4-oxopyrido [2,3-*d*]pyrimidine-7-carboxylate (3c).** Yield: (7.5 mg, 82%); yellow crystals; mp 215 °C; IR (KBr): 1659, 1731, 2984, 3168, 3318 cm<sup>-1</sup>. <sup>1</sup>H NMR (500 MHz, DMSO): δ<sub>H</sub> = 1.32 (t, *J* 7 Hz, 3H, CH<sub>3</sub>), 4.36 (q, *J* 7 Hz, 2H, OCH<sub>2</sub>), 6.95 (s, 2H, NH<sub>2</sub>), 7.57 (d, *J* 8.5 Hz, 2H, Ar), 7.72 (s, 1H, pyridine), 8.21 (d, *J* 8.5 Hz, 2H, Ar). <sup>13</sup>C NMR (125 MHz, DMSO): 13.7, 61.2, 105.4, 106.1, 111.6, 128.8, 1128.9, 135.3, 136.0, 143.4, 154.7, 159.4, 161.8, 167.1. Anal. Calcd for C<sub>16</sub>H<sub>13</sub>ClN<sub>4</sub>O<sub>3</sub>: C, 55.74; H, 3.80; N, 16.25. Found: C, 55.51; H, 3.68; N, 16.42.

**Ethyl-2-amino-5-(4-bromophenyl)-3,4-dihydro-4-oxopyrido [2,3-*d*] pyrimidine-7-carboxylate (3d).** Yield: (9.2 mg, 86%); yellow crystals; mp: 218 °C; IR (KBr): 1683, 1720, 3010, 3145, 3265 cm<sup>-1</sup>. <sup>1</sup>H NMR (500 MHz, DMSO): δ<sub>H</sub> = 1.31 (t, *J* 7 Hz, 3H, CH<sub>3</sub>), 4.34 (q, *J* 7 Hz, 2H, OCH<sub>2</sub>), 6.83 (s, 2H, NH<sub>2</sub>), 7.13 (s, 1H, Pyridine), 7.69 (t, *J* 8 Hz, 2H, Ar), 8.13 (d, *J* 8 Hz, 2H, Ar). <sup>13</sup>C NMR (125 MHz, DMSO): 13.7, 61.2, 95.37, 106.01, 111.9, 112.05, 115.2, 121.3, 129.2, 131.7, 132.3, 143.8, 162.6, 167.5. Anal. Calcd for C<sub>16</sub>H<sub>13</sub>BrN<sub>4</sub>O<sub>3</sub>: C, 49.38; H, 3.37; N, 14.40. Found: C, 49.32; H, 3.31; N, 14.67.

**Ethyl-2-amino-5-(2-chlorophenyl)-3,4-dihydro-4-oxopyrido [2,3-*d*]pyrimidine-7-carboxylate (3e).** Yield: (8mg, 84%); yellow crystals; mp: 215 °C; IR (KBr): 1680, 1741, 2983, 3133, 3310 cm<sup>-1</sup>. <sup>1</sup>H NMR (500 MHz, DMSO): δ<sub>H</sub> = 1.30 (t, *J* 7 Hz, 3H, CH<sub>3</sub>), 4.34 (q, *J* 7 Hz, 2H, OCH<sub>2</sub>), 6.97 (s, 2H, NH<sub>2</sub>), 7.28 (s, 1H, Pyridine), 7.47-7.55 (m, 2H, Ar), 7.57-7.63 (m, 2H, Ar), 11.4 (s, NH). <sup>13</sup>C NMR (125 MHz, DMSO): 13.7, 61.3, 105.1, 106.04, 127.2, 127.4, 129.9, 130.6, 130.7, 130.9, 131.3, 137.9, 142.4, 154.8, 161.4, 167.0. Anal. Calcd for C<sub>16</sub>H<sub>13</sub>ClN<sub>4</sub>O<sub>3</sub>: C, 55.74; H, 3.80; N, 16.25; Found: C, 55.58; H, 3.61; N, 16.43.

**Ethyl-2-amino-5-(2,4-dichlorophenyl)-3,4-dihydro-4-oxopyrido [2,3-*d*]pyrimidine-7-carboxylate (3f).** Yield: (7.3 mg, 81%); yellow crystals; mp: 210 °C; IR (KBr): 1689, 1736, 3133, 3272 cm<sup>-1</sup>. <sup>1</sup>H NMR (500 MHz, DMSO): δ<sub>H</sub> = 1.30 (t, *J* 7 Hz, 3H, CH<sub>3</sub>), 4.35 (q, *J* 7 Hz, 2H, OCH<sub>2</sub>), 7.04 (s, 2H, NH<sub>2</sub>), 7.31 (s, 1H, Pyridine), 7.56 (d, *J* 8 Hz, Ar, 1H), 7.64 (d, *J* 8 Hz, Ar, 1H), 7.75 (s, 1H, Ar). <sup>13</sup>C NMR (125 MHz, DMSO): 13.8, 61.52, 106.35, 115.75, 130.3, 132.17, 132.75, 134.6, 142.6, 155.01, 159.4, 160.4, 167.0, 172. Anal. Calcd for C<sub>16</sub>H<sub>12</sub>Cl<sub>2</sub>N<sub>4</sub>O<sub>3</sub>: C, 50.68; H, 3.19; N, 14.78. Found: C, 50.81; H, 3.32; N, 14.61.



**Ethyl-2-amino-3,4-dihydro-4-oxo-5-*p*-tolylpyrido[2,3-*d*] pyr imidine-7-carboxylate (3g).** Yield: (7 mg, 80%); yellow crystals; mp: 214-215 °C; IR (KBr): 1688, 1718, 3020, 3130, 3230 cm<sup>-1</sup>. <sup>1</sup>H NMR (500 MHz, DMSO): δ<sub>H</sub> = 1.32 (t, *J* 7 Hz, 3H, CH<sub>3</sub>), 1.3 (s, 3H, CH<sub>3</sub>), 4.3 (q, *J* 7 Hz, 2H, OCH<sub>2</sub>), 6.89 (s, 2H, NH<sub>2</sub>), 7.52 (d, *J* 6 Hz, 2H, Ar), 7.69 (s, 1H, Pyridine), 8.18 (d, *J* 6 Hz, 2H, Ar). <sup>13</sup>C NMR (125 MHz, DMSO): 14.30, 16.30, 62.01, 114.3, 114.6, 121.3, 125.6, 128.9, 130.9, 134.2, 139.5, 142.5, 152.2, 156.3, 165.7. Calcd for C<sub>17</sub>H<sub>16</sub>N<sub>4</sub>O<sub>3</sub>: C, 62.95; H, 4.97; N, 17.27. Found: C, 62.55; H, 4.57; N, 16.67.

**Ethyl-2-amino-3,4-dihydro-4-oxo-5-*m*-tolylpyrido[2,3-*d*] pyrimidine-7-carboxylate (3h).** Yield: (6.8 mg, 75%); yellow crystals; mp: 218 °C; IR (KBr): 1676, 1727, 3077, 3176, 3326 cm<sup>-1</sup>. <sup>1</sup>H NMR (500 MHz, DMSO): δ<sub>H</sub> = 1.32 (t, *J* 7 Hz, 3H, CH<sub>3</sub>), 2.4 (s, 3H, CH<sub>3</sub>), 4.35 (q, *J* 7 Hz, 2H, OCH<sub>2</sub>), 6.83 (s, 2H, NH<sub>2</sub>), 7.32 (d, *J* 7 Hz, 2H, Ar), 7.40 (t, *J* 7 Hz, 1H, Ar), 7.66 (s, 1H, Pyridine), 7.97 d, *J* 7 Hz, 1H, Ar), 8.02 (s, 1H, NH). <sup>13</sup>C NMR (125 MHz, DMSO): 14.3, 16.2, 62.0, 115.2, 121.3, 124.7, 125.6, 128.1, 128.8, 128.9, 130.6, 138.4, 138.5, 139.4, 142.5, 156.8, 165.7. Anal. Calcd for C<sub>17</sub>H<sub>16</sub>N<sub>4</sub>O<sub>3</sub>: C, 62.95; H, 4.97; N, 17.27. Found: C, 62.72; H, 4.77; N, 17.45.

**Ethyl-2-amino-3,4-dihydro-5-(4-methoxyphenyl)-4-oxo pyrido[2,3-*d*]pyrimidine-7-carboxylate (3i).** Yield: (6.9 mg, 75%); yellow crystals; mp: 215 °C; IR (KBr): 1682, 1728, 2984, 3170, 3325, 3417 cm<sup>-1</sup>. <sup>1</sup>H NMR (500 MHz, DMSO): δ<sub>H</sub> = 1.32 (t, *J* 7 Hz, 3H, CH<sub>3</sub>), 3.4 (s, 3H, OCH<sub>3</sub>), 4.3 (q, *J* 7 Hz, 2H, OCH<sub>2</sub>), 6.8 (s, 2H, NH<sub>2</sub>), 7.5 (d, *J* 6 Hz, 2H, Ar), 7.6 (s, 1H, Pyridine), 8.0 (d, *J* 6 Hz, 2H, Ar), 11.0 (s, 1H, NH). <sup>13</sup>C NMR (125 MHz, DMSO): 13.7, 60.0, 61.2, 110.6, 127.1, 127.2, 127.7, 128.8, 129.6, 130.5, 137.2, 143.3, 154.8, 160.7, 167.3. Anal. Calcd for C<sub>17</sub>H<sub>16</sub>N<sub>4</sub>O<sub>4</sub>: C, 59.99; H, 4.74; N, 16.46. Found: C, 59.81; H, 4.60; N, 16.33.

**Ethyl-2-amino-3,4-dihydro-5-(3,4-dimethoxyphenyl)-4-oxo pyrido[2,3-*d*]pyrimidine-7-carboxylate (3j).** Yield: (6.4 mg, 73%); yellow crystals; mp: 218 °C; IR (KBr): 1657, 1724, 2837, 2925, 3153, 3360 cm<sup>-1</sup>. <sup>1</sup>H NMR (500 MHz, DMSO): δ<sub>H</sub> = 1.32 (t, *J* 7 Hz, 3H, CH<sub>3</sub>), 3.84 (s, OCH<sub>3</sub>), 3.87 (OCH<sub>3</sub>), 4.35 (q, *J* 7 Hz, 2H, OCH<sub>2</sub>), 7.07 (d, *J* 8 Hz, 1H, Ar), 7.68 (s, 1H, Pyridine), 7.79 (d, *J* 8 Hz, 2H, Ar), 7.80 (s, 1H, NH). <sup>13</sup>C NMR (125 MHz, DMSO): 13.7, 50.6, 55.56, 61.2, 105.2, 110.3, 112.1, 112.54, 110.7, 120.5, 129.8, 143.1, 148.9, 151.0, 154.8, 160.4, 167.4, 171.8. Anal. Calcd for: C<sub>18</sub>H<sub>18</sub>N<sub>4</sub>O<sub>5</sub>: C, 58.37; H, 4.90; N, 15.13. Found: C, 58.55; H, 4.76; N, 15.32.

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## Supplementary Material

Supplementary data associated with this manuscript, consisting of copies of <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra, can be found in the online version.

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