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**SYNTHESIS OF 6,7-DIHYDROPYRIDO[2,3-*d*]PYRIMIDIN-5(8*H*)-ONE  
DERIVATIVES BASED ON THE REACTION OF  
1-(4-CHLOROPYRIMIDIN-5-YL)ALK-2-EN-1-ONE DERIVATIVES  
WITH PRIMARY AMINES**

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**Abstract** – A convenient sequence for the synthesis of 6,7-dihydropyrido[2,3-*d*]pyrimidin-5(8*H*)-one derivatives has been developed. Thus, treatment of 4-chloro-6-methoxy-2-(methylsulfanyl)pyrimidine with lithium diisopropylamide (LDA) generates 4-chloro-5-lithio-6-methoxy-2-(methylsulfanyl)pyrimidine, which are allowed to react with  $\alpha,\beta$ -unsaturated aldehydes to give the corresponding 1-(4-chloropyrimidin-5-yl)alk-2-en-1-ol derivatives. Oxidation of these alkenols with activated manganese(IV) oxide provides 1-(4-chloropyrimidin-5-yl)alk-2-en-1-one derivatives, of which reaction with a variety of primary amines constitutes tetrahydropyridinone structure to give the desired products.

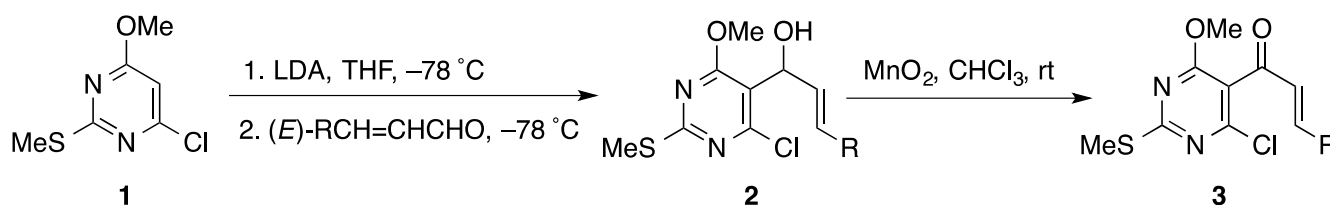
## INTRODUCTION

A number of pyrido[2,3-*d*]pyrimidin-5(8*H*)-one derivatives have recently been synthesized<sup>1,2</sup> and some of them have been reported to exhibit a variety of biological activities.<sup>2</sup> However, only few reports on the synthesis of 6,7-dihydropyrido[2,3-*d*]pyrimidin-5(8*H*)-one derivatives, which are also of biological importance. As the sole example, to the best of our knowledge, Assy and Moustafa prepared some derivatives by condensation of 1-[4-(alkylamino)pyrimidin-5-yl]ethanones with benzaldehyde.<sup>3</sup> On the other hand, we have recently reported methods for the synthesis of several pyrimidine-fused heterocycles

utilizing 4-chloro-6-methoxy-2-(methylsulfanyl)pyrimidine (**1**), readily available from 4,6-dichloro-2-(methylsulfanyl)pyrimidine (DCSMP).<sup>4</sup> In continuation of these studies, we embarked upon development of a facile method for the preparation of 6,7-dihydropyrido[2,3-*d*]pyrimidin-5(8*H*)-one derivatives from **1**. This paper describes that 7,8-disubstituted 4-methoxy-2-(methylsulfanyl)-6,7-dihydropyrido[2,3-*d*]pyrimidin-5(8*H*)-ones (**4**), (**5**), (**7**), and (**8**) can be prepared by an easy three-step sequence from **1**.

## RESULTS AND DISCUSSION

From the outset, we envisioned that the reaction of 1-(4-chloropyrimidin-5-yl)alk-2-en-1-one derivatives (**3**) with primary amines would provide the desired 6,7-dihydropyrido[2,3-*d*]pyrimidin-5(8*H*)-one derivatives (**4**). First to be carried out was the preparation of **3** by the treatment of 4-chloro-5-lithio-6-methoxy-2-(methylsulfanyl)pyrimidine, generated from 4-chloro-6-methoxy-2-(methylsulfanyl)pyrimidine (**1**) on treatment with lithium diisopropylamide (LDA) in THF at  $-78\text{ }^{\circ}\text{C}$ ,<sup>4</sup> with  $\alpha,\beta$ -unsaturated aldehydes, followed by the oxidation of the resulting 1-(4-chloropyrimidin-5-yl)alk-2-en-1-ol derivatives (**2**) with activated manganese(IV) oxide (Scheme 1). This sequence could be achieved in uneventful fashion to provide **3** in good yields as compiled in Table 1.



Scheme 1

**Table 1.** Preparation of 1-(pyrimidin-4-yl)alk-2-en-1-ones (**3**)

Entry	R	<b>2</b>	Yield/% <sup>a</sup>	<b>3</b>	Yield/% <sup>a</sup>
1	Me	<b>2a</b>	90	<b>3a</b>	89
2	Et	<b>2b</b>	95	<b>3b</b>	81
3	Ph	<b>2c</b>	73 <sup>b</sup>	<b>3c</b>	87
4	4-ClC <sub>6</sub> H <sub>4</sub>	<b>2d</b>	78 <sup>b</sup>	<b>3d</b>	82
5	4-MeOC <sub>6</sub> H <sub>4</sub>	<b>2e</b>	94 <sup>b</sup>	<b>3e</b>	91

<sup>a</sup> Yields of isolated products. <sup>b</sup> See ref. 4b.

The pyrimidinyl enones (**3**), thus obtained, were then subjected to the reaction with primary amines in DMF. First, the reactions of **3a** (R = Me) with aliphatic primary amines were carried out (Scheme 2). They proceeded quickly even at  $0\text{ }^{\circ}\text{C}$  and were over in less than 1 h to afford the corresponding desired products (**4a-4d**) in good yields (Table 2, Entries 1-4). When phenylhydrazine was used, the reaction also proceeded at  $0\text{ }^{\circ}\text{C}$ . However, it resulted in the formation of a rather complicated mixture of products and

only moderate yield of the desired products (**4e**) was isolated (Entry 5). The treatment of **3a** with benzenamine was initially conducted at 0 °C. However, no desired product (**4f**) was formed. When the temperature was raised to 40 °C, the reaction proceeded in a satisfactory manner to produce **4f** in fair yield (Entry 6). The reaction of **3b** (R = Et) with butanamine also proceeded at 0 °C. However, it required much longer reaction time and the yield of the corresponding product (**4g**) was somewhat lower than that of **4a** (Entry 7). In the production of **4** from **3**, the conjugate addition of primary amine is thought to take place initially, resulting in the formation of the corresponding  $\beta$ -(alkylamino) ketones. This is followed by the  $S_NAr$  displacement of the chlorine on the pyrimidine ring with the amino nitrogen of the corresponding adducts to give rise to **4**.



Scheme 2

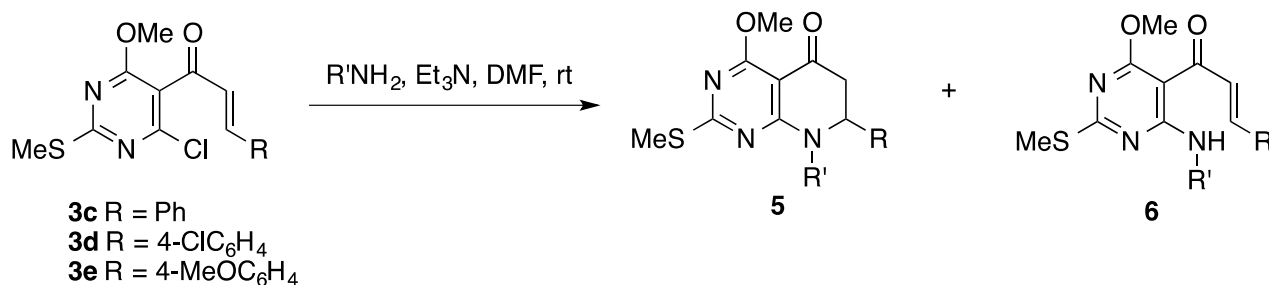
**Table 2.** Preparation of 7-alkyl-6,7-dihydropyrido[2,3-*d*]pyrimidin-5(8*H*)-one derivatives (**4**)

Entry	<b>3</b>	R'	Temp/°C	Time/h	<b>4</b>	Yield/% <sup>a</sup>
1	<b>3a</b> (R = Me)	<i>n</i> -Bu	0	0.5	<b>4a</b>	85
2	<b>3a</b>	Bn	0	0.75	<b>4b</b>	92
3	<b>3a</b>	MeO(CH <sub>2</sub> ) <sub>2</sub>	0	0.5	<b>4c</b>	89
4	<b>3a</b>	cyclopropyl	0	0.5	<b>4d</b>	93
5	<b>3a</b>	PhNH	0	1	<b>4e</b>	41
6	<b>3a</b>	Ph	40	3	<b>4f</b>	74
7	<b>3b</b> (R = Et)	<i>n</i> -Bu	0	2	<b>4g</b>	70

<sup>a</sup> Yields of isolated products.

Next, the reactions of  $\beta$ -aryl enone derivatives (**3c-e**) with primary amines were examined. They proceeded at room temperature to give the desired pyridopyrimidinone derivatives (**5**) accompanying the formation of the corresponding 1-[4-(alkylamino)pyrimidin-5-yl]-3-arylprop-2-en-1-ones (**6**) as shown in Scheme 3. The results are summarized in Table 3, which indicate that the use of a small amine, such as methanamine, and the substitution of the electron-withdrawing group on the benzene ring of the substrate shortened the reaction times and favored the formation of **5**. It should be noted that the prolonged time of each reaction did not affect the ratio of the products at all. Moreover, when isolated **6a** was subjected to the same reaction conditions, transformation into **5a** did not occur. These observations indicate that the

production of **5** through the initial formation of **6**, followed by intramolecular conjugate addition, is ultimately ruled out.

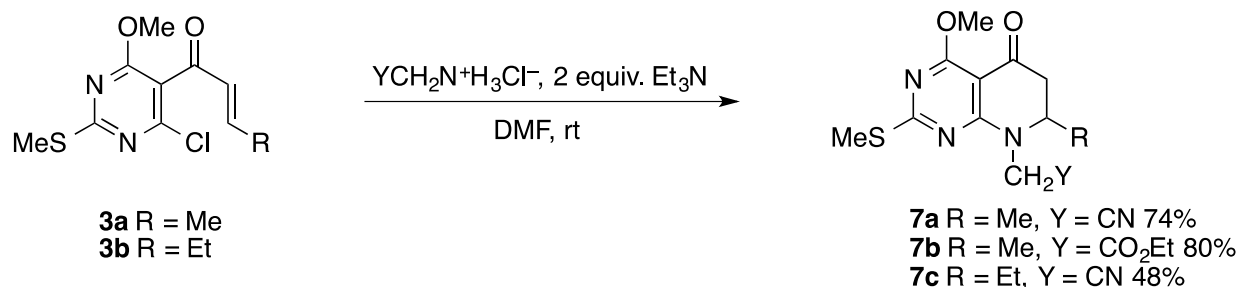


Scheme 3

**Table 3.** Preparation of 7-aryl-6,7-dihydropyrido[2,3-*d*]pyrimidin-5(8*H*)-one derivatives (**5**)

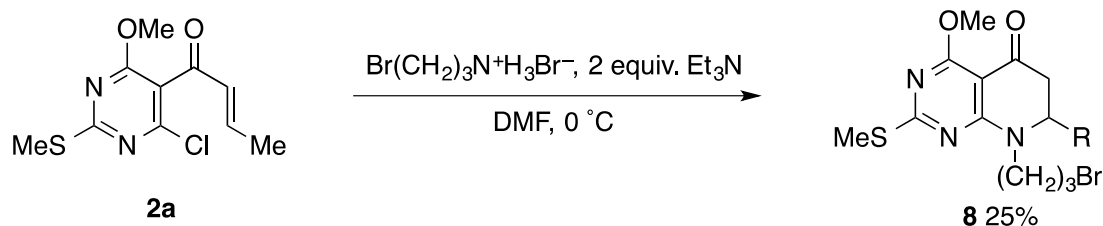
Entry	<b>3</b>	R'	Time/h	<b>5</b>	Yield/% <sup>a</sup>	<b>6</b>	Yield/% <sup>a</sup>
1	<b>3c</b> (R = Ph)	Ph(CH <sub>2</sub> ) <sub>2</sub>	7	<b>5a</b>	56	<b>6a</b>	25
2	<b>3c</b>	Me	5	<b>5b</b>	68	<b>6b</b>	11
3	<b>3d</b> (R = 4-ClC <sub>6</sub> H <sub>4</sub> )	Me	4	<b>5c</b>	78	<b>6c</b>	8
4	<b>3e</b> (R = 4-MeOC <sub>6</sub> H <sub>4</sub> )	Ph(CH <sub>2</sub> ) <sub>2</sub>	10	<b>5d</b>	12	<b>6d</b>	71
5	<b>3e</b>	Me	8	<b>5e</b>	43	<b>6e</b>	42

<sup>a</sup> Yields of isolated products.



Scheme 4

Subsequently, in order to demonstrate the present synthesis more efficient, the reactions of  $\beta$ -alkenone derivatives (**3a**) and (**3b**) with 2-aminoacetonitrile hydrochloride or glycine ethyl ester hydrochloride in the presence of 2 equivalents of triethylamine were examined. As shown in Scheme 4, they proceeded at room temperature to provide the corresponding pyridopyrimidinone derivatives (**7**). While the yields of the products (**7a**) and (**7b**) from **3a** were relatively good, the reaction of **3b** with 2-aminoacetonitrile hydrochloride afforded the corresponding product (**7c**) in a considerably lower yield. Similarly, the reaction of **3a** with 3-bromopropanamine hydrobromide in the presence of 2 equivalents of triethylamine at 0 °C was carried out. Unfortunately, however, it resulted in the formation of a rather intractable mixture of products, from which only a low yield of the desired product (**8**) was isolated (Scheme 5). This may be due to the liability of the terminal bromide of the product.



Scheme 5

In conclusion, a convenient synthesis of 6,7-dihydropyrido[2,3-*d*]pyrimidin-5(8*H*)-one derivatives has been realized. The ready availability of the starting materials as well as the simple operations makes this method attractive. Further experiments aimed at developing methodology for the preparation of other pyrimidine-fused heterocycles utilizing the precursors in this work are currently under active investigation.

## EXPERIMENTAL

All melting points were obtained on a Laboratory Devices MEL-TEMP II melting apparatus and are uncorrected. IR spectra were recorded with a Perkin–Elmer Spectrum65 FTIR spectrophotometer.  $^1\text{H}$  NMR and  $^{13}\text{C}$  NMR spectra were recorded in  $\text{CDCl}_3$  using TMS as an internal reference with a JEOL ECP500 FT NMR spectrometer operating at 500 and 125 MHz, respectively. High-resolution MS spectra (ESI, positive) or (EI, TOF; 70eV) were measured by a Thermo Scientific Exactive or a JEOL JMS-T100GCV spectrometer, respectively. Elemental analyses were performed with Elementar Vario EL II instrument. TLC was carried out on Merck Kieselgel 60 PF<sub>254</sub>. Column chromatography was performed using WAKO GEL C-200E. All of the organic solvents used in this study were dried over appropriate drying agents and distilled prior to use.

**Starting Materials.** 4-Chloro-6-methoxy-2-(methylsulfanyl)pyrimidine (**1**) was prepared following the reported procedure.<sup>4</sup> *n*-BuLi was supplied by Asia Lithium Corporation. All other chemicals used in this study were commercially available.

**Pyrimidinyl Alkenols (2).** These compounds were prepared according to the procedure previously reported for the preparation of **2c–e**.<sup>4b</sup> The physical, spectral, and analytical data for new compounds follow.

**(*E*)-1-[4-Chloro-6-methoxy-2-(methylsulfanyl)pyrimidin-5-yl]but-2-en-1-ol (2a):** a white solid; mp 63–65 °C (hexane); IR (KBr) 3346, 1663  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR  $\delta$  1.70 (d,  $J = 5.4$  Hz, 3H), 2.55 (s, 3H), 2.99 (d,  $J = 10.7$  Hz, 1H), 4.07 (s, 3H), 5.45 (dd,  $J = 10.7, 5.4$  Hz, 1H), 5.68–5.79 (m, 2H). Anal. Calcd for  $\text{C}_{10}\text{H}_{13}\text{ClN}_2\text{O}_2\text{S}$ : C, 46.06; H, 5.03; N, 10.74. Found: C, 46.12; H, 5.23; N, 10.66.

**(E)-1-[4-Chloro-6-methoxy-2-(methylsulfanyl)pyrimidin-5-yl]pent-2-en-1-ol (2b):** a colorless oil;  $R_f$  0.33 (AcOEt/hexane 1:5); IR (neat) 3419, 1657  $\text{cm}^{-1}$ ;  $^1\text{H NMR}$   $\delta$  0.99 (t,  $J = 6.9$  Hz, 3H), 2.03–2.08 (m, 2H), 2.55 (s, 3H), 3.00 (d,  $J = 10.3$  Hz, 1H), 4.07 (s, 3H), 5.45–5.48 (m, 1H), 5.69–5.78 (m, 2H). Anal. Calcd for  $\text{C}_{11}\text{H}_{15}\text{ClN}_2\text{O}_2\text{S}$ : C, 48.08; H, 5.50; N, 10.20. Found: C, 48.09; H, 5.53; N, 10.06.

**Typical Procedure for the Preparation of Pyrimidinyl Ketones (3).** **(E)-1-[4-Chloro-6-methoxy-2-(methylsulfanyl)pyrimidin-5-yl]but-2-en-1-one (3a).** A mixture of **2a** (0.48 g, 1.9 mmol) and activated  $\text{MnO}_2$  (1.6 g, 19 mmol) in  $\text{CHCl}_3$  (5 mL) was stirred at rt for 2 h. The mixture was filtered through a Celite® pad under reduced pressure and the filtrate was concentrated by evaporation. The residual solid was recrystallized from hexane/ $\text{CH}_2\text{Cl}_2$  to give **3a** (0.43 g, 89%); a white solid; mp 99–101 °C; IR (KBr) 1652, 1635  $\text{cm}^{-1}$ ;  $^1\text{H NMR}$   $\delta$  1.97 (dd,  $J = 6.9, 1.5$  Hz, 3H), 2.57 (s, 3H), 3.99 (s, 3H), 6.33 (dd,  $J = 16.1, 1.5$  Hz, 1H), 6.71 (dq,  $J = 16.1, 6.9$  Hz, 1H). Anal. Calcd for  $\text{C}_{10}\text{H}_{11}\text{ClN}_2\text{O}_2\text{S}$ : C, 46.42; H, 4.29; N, 10.83. Found: C, 46.38; H, 4.19; N, 10.90.

**(E)-1-[4-Chloro-6-methoxy-2-(methylsulfanyl)pyrimidin-5-yl]pent-2-en-1-one (3b):** a white solid; mp 51–52 °C (hexane/ $\text{CH}_2\text{Cl}_2$ ); IR (KBr) 1655, 1635  $\text{cm}^{-1}$ ;  $^1\text{H NMR}$   $\delta$  1.10 (t,  $J = 7.4$  Hz, 3H), 2.30–2.33 (m, 2H), 2.58 (s, 3H), 3.99 (s, 3H), 6.30 (d,  $J = 16.0$  Hz, 1H), 6.75 (dd,  $J = 16.0, 6.3$  Hz, 1H). Anal. Calcd for  $\text{C}_{11}\text{H}_{13}\text{ClN}_2\text{O}_2\text{S}$ : C, 48.44; H, 4.80; N, 10.27. Found: C, 48.29; H, 4.86; N, 10.11.

**(E)-1-[4-Chloro-6-methoxy-2-(methylsulfanyl)pyrimidin-5-yl]-3-phenylprop-2-en-1-one (3c):** a white solid; mp 120–122 °C (hexane/ $\text{CH}_2\text{Cl}_2$ ); IR (KBr) 1653, 1624  $\text{cm}^{-1}$ ;  $^1\text{H NMR}$   $\delta$  2.61 (s, 3H), 4.01 (s, 3H), 6.94 (d,  $J = 16.1$  Hz, 1H), 7.39 (d,  $J = 16.1$  Hz, 1H), 7.41–7.43 (m, 3H), 7.56 (dd,  $J = 7.6, 1.5$  Hz, 2H). Anal. Calcd for  $\text{C}_{15}\text{H}_{13}\text{ClN}_2\text{O}_2\text{S}$ : C, 56.16; H, 4.08; N, 8.73. Found: C, 55.98; H, 4.08; N, 8.74.

**(E)-1-[4-Chloro-6-methoxy-2-(methylsulfanyl)pyrimidin-5-yl]-3-(4-chlorophenyl)prop-2-en-1-one (3d):** a white solid; mp 136–138 °C (hexane/ $\text{CH}_2\text{Cl}_2$ ); IR (KBr) 1683, 1651, 1607  $\text{cm}^{-1}$ ;  $^1\text{H NMR}$   $\delta$  2.60 (s, 3H), 4.01 (s, 3H), 6.90 (d,  $J = 16.0$  Hz, 1H), 7.36 (d,  $J = 16.0$  Hz, 1H), 7.39 (d,  $J = 8.6$  Hz, 2H), 7.49 (d,  $J = 8.6$  Hz, 2H). Anal. Calcd for  $\text{C}_{15}\text{H}_{12}\text{Cl}_2\text{N}_2\text{O}_2\text{S}$ : C, 50.72; H, 3.41; N, 7.89. Found: C, 50.53; H, 3.45; N, 7.84.

**(E)-1-[4-Chloro-6-methoxy-2-(methylsulfanyl)pyrimidin-5-yl]-3-(4-methoxyphenyl)prop-2-en-1-one (3e):** a white solid; mp 133–135 °C (hexane/ $\text{CH}_2\text{Cl}_2$ ); IR (KBr) 1646  $\text{cm}^{-1}$ ;  $^1\text{H NMR}$   $\delta$  2.60 (s, 3H), 3.86 (s, 3H), 4.00 (s, 3H), 6.82 (d,  $J = 16.1$  Hz, 1H), 6.93 (d,  $J = 9.2$  Hz, 2H), 7.33 (d,  $J = 16.1$  Hz, 1H), 7.52 (d,  $J = 9.2$  Hz, 2H). Anal. Calcd for  $\text{C}_{16}\text{H}_{15}\text{ClN}_2\text{O}_3\text{S}$ : C, 54.78; H, 4.31; N, 7.99. Found: C, 54.49; H, 4.04; N, 8.24.

**General Procedure for the Preparation of Pyridopyrimidinones (4) and (5).** To a stirred solution of **3** (1.0 mmol) and  $\text{Et}_3\text{N}$  (1.0 mmol) in DMF (4 mL) at 0 °C was added an amine (1.0 mmol) dropwise. Stirring was continued at the temperature indicated in Table 1 or Scheme 3 until **3** had been consumed completely (TLC,  $\text{SiO}_2$ , AcOEt/hexane 1:1, see Tables 2 and 3). Water (20 mL) was added and the

mixture was extracted with AcOEt (3 × 15 mL). The combined extracts were washed with water (3 × 15 mL) and brine (15 mL), dried (Na<sub>2</sub>SO<sub>4</sub>), and concentrated by evaporation. The residue was purified by column chromatography (AcOEt/hexane 1:1) on SiO<sub>2</sub> to afford **4** or **5**.

**8-Butyl-4-methoxy-7-methyl-2-(methylsulfanyl)-6,7-dihydropyrido[2.3-*d*]pyridin-5(8*H*)-one (4a):** a colorless viscous oil; *R<sub>f</sub>* 0.31 (AcOEt/hexane 1:1); IR (neat) 1678 cm<sup>-1</sup>; <sup>1</sup>H NMR δ 0.97 (t, *J* = 7.6 Hz, 3H), 1.20 (d, *J* = 6.1 Hz, 3H), 1.35–1.43 (m, 2H), 1.63–1.72 (m, 2H), 2.39 (dd, *J* = 16.1, 2.3 Hz, 1H), 2.51 (s, 3H), 2.85 (dd, *J* = 16.1, 6.1 Hz, 1H), 3.02–3.07 (m, 1H), 3.74–3.77 (m, 1H), 4.03 (s, 3H), 4.20–4.26 (m, 1H); <sup>13</sup>C NMR δ 13.91, 14.09, 16.23, 20.15, 30.50, 43.79, 47.19, 51.38, 54.52, 93.81, 161.20, 166.90, 175.09, 189.27. HR-MS (ESI). Calcd for C<sub>14</sub>H<sub>22</sub>N<sub>3</sub>O<sub>2</sub>S (M+H): 296.1432. Found: *m/z* 296.1424. Anal. Calcd for C<sub>14</sub>H<sub>21</sub>N<sub>3</sub>O<sub>2</sub>S: C, 56.92; H, 7.17; N, 14.22. Found: C, 56.80; H, 7.25; N, 14.15.

**4-Methoxy-7-methyl-2-(methylsulfanyl)-8-(2-phenylmethyl)-6,7-dihydropyrido[2.3-*d*]pyridin-5(8*H*)-one (4b):** a white solid; mp 96–98 °C (hexane/CH<sub>2</sub>Cl<sub>2</sub>); IR (KBr) 1678 cm<sup>-1</sup>; <sup>1</sup>H NMR δ 1.18 (d, *J* = 6.9 Hz, 3H), 2.35 (dd, *J* = 16.0, 2.3 Hz, 1H), 2.46 (s, 3H), 2.80 (dd, *J* = 16.0, 6.1 Hz, 1H), 3.70–3.76 (m, 1H), 4.06 (s, 3H), 4.20 (d, *J* = 15.3 Hz, 1H), 5.68 (d, *J* = 15.3 Hz, 1H), 7.28–7.31 (m, 3H), 7.35 (t, *J* = 7.6 Hz, 2H); <sup>13</sup>C NMR δ 14.18, 15.83, 43.78, 49.63, 50.35, 54.64, 93.93, 127.49, 127.60, 128.75, 137.60, 161.57, 167.02, 175.45, 189.17. HR-MS (ESI). Calcd for C<sub>17</sub>H<sub>20</sub>N<sub>3</sub>O<sub>2</sub>S (M+H): 330.1276. Found: *m/z* 330.1274. Anal. Calcd for C<sub>17</sub>H<sub>19</sub>N<sub>3</sub>O<sub>2</sub>S: C, 61.98; H, 5.81; N, 12.76. Found: C, 61.91; H, 5.71; N, 12.79.

**4-Methoxy-8-(2-methoxyethyl)-7-methyl-2-(methylsulfanyl)-6,7-dihydropyrido[2.3-*d*]pyridin-5(8*H*)-one (4c):** a white solid; mp 110–112 °C (hexane/CH<sub>2</sub>Cl<sub>2</sub>); IR (KBr) 1683 cm<sup>-1</sup>; <sup>1</sup>H NMR δ 1.19 (d, *J* = 6.9 Hz, 3H), 2.36 (dd, *J* = 15.2, 2.3 Hz, 1H), 2.50 (s, 3H), 2.91 (dd, *J* = 15.2, 6.1 Hz, 1H), 3.27–3.32 (m, 1H), 3.37 (s, 3H), 3.62–3.64 (m, 2H), 3.88–3.94 (m, 1H), 4.03 (s, 3H), 4.34 (dt, *J* = 11.6, 4.6 Hz, 1H); <sup>13</sup>C NMR δ 14.10, 16.03, 43.61, 47.32, 52.47, 54.54, 59.02, 71.20, 94.00, 161.15, 166.79, 175.07, 189.55. HR-MS (ESI). Calcd for C<sub>13</sub>H<sub>20</sub>N<sub>3</sub>O<sub>3</sub>S (M+H): 298.1225. Found: *m/z* 298.1217. Anal. Calcd for C<sub>13</sub>H<sub>19</sub>N<sub>3</sub>O<sub>3</sub>S: C, 52.51; H, 6.44; N, 14.13. Found: C, 52.58; H, 6.43; N, 14.16.

**8-Cyclopropyl-4-methoxy-7-methyl-2-(methylsulfanyl)-6,7-dihydropyrido[2.3-*d*]pyridin-5(8*H*)-one (4d):** a white solid; mp 100–102 °C (hexane/CH<sub>2</sub>Cl<sub>2</sub>); IR (KBr) 1681 cm<sup>-1</sup>; <sup>1</sup>H NMR δ 0.66–0.70 (m, 1H), 0.80–0.83 (m, 2H), 1.07–1.13 (m, 1H), 1.24 (d, *J* = 6.9 Hz, 3H), 2.41 (dd, *J* = 16.0, 1.5 Hz, 1H), 2.56 (s, 3H), 2.73–2.78 (m, 1H), 2.81 (dd, *J* = 16.0, 6.9 Hz, 1H), 3.89–3.91 (m, 1H), 4.04 (s, 3H); <sup>13</sup>C NMR δ 6.23, 10.51, 14.18, 15.66, 30.18, 44.46, 52.55, 54.62, 94.66, 163.54, 166.89, 175.10, 189.74. HR-MS (ESI). Calcd for C<sub>13</sub>H<sub>18</sub>N<sub>3</sub>O<sub>2</sub>S (M+H): 280.1119. Found: *m/z* 280.1118. Anal. Calcd for C<sub>13</sub>H<sub>17</sub>N<sub>3</sub>O<sub>2</sub>S: C, 55.89; H, 6.13; N, 15.04. Found: C, 55.97; H, 6.15; N, 15.05.

**4-Methoxy-7-methyl-2-(methylsulfanyl)-8-(phenylamino)-6,7-dihydropyrido[2.3-*d*]pyridin-5(8*H*)-one (4e):** a white solid; mp 176–178 °C (hexane/CH<sub>2</sub>Cl<sub>2</sub>); IR (KBr) 3290, 1664, 1606 cm<sup>-1</sup>; <sup>1</sup>H NMR δ

1.35 (d,  $J = 6.1$  Hz, 3H), 2.29 (s, 3H), 2.65 (dd,  $J = 16.0, 4.6$  Hz, 1H), 3.12 (d,  $J = 16.0, 6.1$  Hz, 1H), 4.01–4.07 (m, including s at 4.05, 4H), 6.69 (s, 1H), 6.90 (d,  $J = 7.6$  Hz, 2H), 6.95 (t,  $J = 7.6$  Hz, 1H), 7.27 (t,  $J = 7.6$  Hz, 2H);  $^{13}\text{C}$  NMR  $\delta$  14.14, 16.16, 44.72, 54.93, 55.31, 94.43, 113.62, 121.50, 129.27, 147.75, 153.05, 166.75, 176.24, 188.74. HR-MS (ESI). Calcd for  $\text{C}_{16}\text{H}_{19}\text{N}_4\text{O}_2\text{S}$  (M+H): 331.1228. Found:  $m/z$  331.1222. Anal. Calcd for  $\text{C}_{16}\text{H}_{18}\text{N}_4\text{O}_2\text{S}$ : C, 58.16; H, 5.49; N, 16.96. Found: C, 58.04; H, 5.68; N, 16.90.

**4-Methoxy-7-methyl-2-(methylsulfanyl)-8-phenyl-6,7-dihydropyrido[2.3-*d*]pyridin-5(8*H*)-one (4f)**: a white solid; mp 161–163 °C (hexane/ $\text{CH}_2\text{Cl}_2$ ); IR (KBr) 1686  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR  $\delta$  1.26 (d,  $J = 6.1$  Hz, 3H), 2.13 (s, 3H), 2.57 (dd,  $J = 16.0, 4.6$  Hz, 1H), 3.08 (dd,  $J = 16.0, 6.1$  Hz, 1H), 4.05 (s, 3H), 4.13–4.19 (m, 1H), 7.25 (d,  $J = 7.6$  Hz, 2H), 7.33 (t,  $J = 7.6$  Hz, 1H), 7.43 (t,  $J = 7.6$  Hz, 2H);  $^{13}\text{C}$  NMR  $\delta$  13.82, 17.19, 44.57, 54.55, 54.73, 94.25, 127.16, 128.02, 128.95, 142.07, 161.80, 167.01, 175.05, 189.26. HR-MS (ESI). Calcd for  $\text{C}_{16}\text{H}_{18}\text{N}_3\text{O}_2\text{S}$  (M+H): 316.1119. Found:  $m/z$  316.1114. Anal. Calcd for  $\text{C}_{16}\text{H}_{17}\text{N}_3\text{O}_2\text{S}$ : C, 60.93; H, 5.43; N, 13.32. Found: C, 60.94; H, 5.50; N, 13.30.

**8-Butyl-7-ethyl-4-methoxy-2-(methylsulfanyl)-6,7-dihydropyrido[2.3-*d*]pyridin-5(8*H*)-one (4g)**: a pale-yellow viscous oil;  $R_f$  0.32 (AcOEt/hexane 1:3); IR (neat) 1677  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR  $\delta$  0.91 (t,  $J = 7.4$  Hz, 3H), 0.97 (t,  $J = 7.4$  Hz, 3H), 1.35–1.42 (m, 2H), 1.62–1.69 (m, 4H), 2.51 (s, 3H), 2.56 (dd,  $J = 16.0, 1.7$  Hz, 1H), 2.79 (dd,  $J = 16.0, 6.3$  Hz, 1H), 2.95–3.00 (m, 1H), 3.45–3.49 (m, 1H), 4.02 (s, 3H), 4.30–4.34 (m, 1H);  $^{13}\text{C}$  NMR  $\delta$  10.24, 13.93, 14.09, 20.19, 23.12, 30.57, 40.63, 48.03, 54.50, 57.35, 93.98, 161.41, 166.81, 175.03, 189.33. HR-MS (EI). Calcd for  $\text{C}_{15}\text{H}_{23}\text{N}_3\text{O}_2\text{S}$  (M): 309.1511. Found:  $m/z$  309.1510. Anal. Calcd for  $\text{C}_{15}\text{H}_{23}\text{N}_3\text{O}_2\text{S}$ : C, 58.23; H, 7.49; N, 13.68; S, 10.36. Found: C, 57.89; H, 7.40; N, 13.66; S, 10.47.

**4-Methoxy-2-(methylsulfanyl)-7-phenyl-8-(2-phenylethyl)-6,7-dihydropyrido[2.3-*d*]pyridin-5(8*H*)-one (5a)**. This compound was obtained accompanying **6a**. A white solid; mp 110–112 °C (hexane/ $\text{CH}_2\text{Cl}_2$ ); IR (KBr) 1678  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR  $\delta$  2.60 (s, 3H), 2.63 (dd,  $J = 16.0, 3.1$  Hz, 1H), 2.87–2.95 (m, 2H), 3.02–3.08 (m, 1H), 3.10–3.16 (m, 1H), 4.03 (s, 3H), 4.39 (dd,  $J = 6.9, 3.1$  Hz, 1H), 4.51–4.56 (m, 1H), 7.02 (dd,  $J = 7.6, 1.5$  Hz, 2H), 7.17 (d,  $J = 6.9$  Hz, 2H), 7.23–7.28 (m, 4H), 7.30 (dd,  $J = 7.6, 6.9$  Hz, 2H);  $^{13}\text{C}$  NMR  $\delta$  14.24, 34.40, 44.36, 50.54, 54.59, 60.17, 94.87, 126.07, 126.64, 128.11, 128.60, 128.83, 129.01, 138.36, 138.89, 162.70, 166.71, 175.57, 183.04. HR-MS (ESI). Calcd for  $\text{C}_{23}\text{H}_{24}\text{N}_3\text{O}_2\text{S}$  (M+H): 406.1589. Found:  $m/z$  406.1584. Anal. Calcd for  $\text{C}_{23}\text{H}_{23}\text{N}_3\text{O}_2\text{S}$ : C, 68.12; H, 5.72; N, 10.36; S, 7.91. Found: C, 67.96; H, 5.65; N, 10.34; S, 7.92.

**1-[3-Methoxy-2-(methylsulfanyl)-5-[(2-phenylethyl)amino]pyrimidin-4-yl]-3-phenylprop-2-en-1-one (6a)**: a yellow solid; mp 152–154 °C (hexane/ $\text{CH}_2\text{Cl}_2$ ); IR (KBr) 3222, 1636  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR  $\delta$  2.56 (s, 3H), 2.95 (t,  $J = 7.6$  Hz, 2H), 3.81 (q,  $J = 7.6$  Hz, 2H), 4.07 (s, 3H), 7.23–7.26 (m, 3H), 7.32 (t,  $J = 7.6$  Hz, 2H), 7.37–7.42 (m, 3H), 7.58 (dd,  $J = 7.6, 1.5$  Hz, 2H), 7.62 (d,  $J = 15.3$  Hz, 1H), 7.73 (d,  $J = 15.3$  Hz, 1H),

10.04 (br s, 1H). Anal. Calcd for  $C_{23}H_{23}N_3O_2S$ : C, 68.12; H, 5.72; N, 10.36. Found: C, 68.14; H, 6.01; N, 10.22.

**4-Methoxy-8-methyl-2-(methylsulfanyl)-7-phenyl-6,7-dihydropyrido[2.3-*d*]pyridin-5(8*H*)-one (5b).**

This compound was obtained accompanying **6b**. A white solid; mp 164–165 °C (hexane/ $CH_2Cl_2$ ); IR (KBr) 1668  $cm^{-1}$ ;  $^1H$  NMR  $\delta$  2.56 (s, 3H), 2.78 (dd,  $J = 16.0, 3.4$  Hz, 1H), 3.11 (dd,  $J = 16.0, 6.9$  Hz, 1H), 3.21 (s, 3H), 4.07 (s, 3H), 4.72 (dd,  $J = 6.9, 3.4$  Hz, 1H), 7.11 (dd,  $J = 8.0, 1.7$  Hz, 2H), 7.25–7.32 (m, 3H);  $^{13}C$  NMR  $\delta$  14.19, 35.97, 44.69, 54.59, 61.48, 94.89, 126.02, 128.13, 129.09, 138.30, 163.19, 166.68, 175.56, 188.17. HR-MS (EI). Calcd for  $C_{16}H_{17}N_3O_2S$  (M): 315.1041. Found:  $m/z$  315.1053. Anal. Calcd for  $C_{16}H_{17}N_3O_2S$ : C, 60.93; H, 5.43; N, 13.32. Found: C, 60.86; H, 5.49; N, 13.17.

**1-[3-Methoxy-5-(methylamino)-2-(methylsulfanyl)]pyrimidin-4-yl]-3-phenylprop-2-en-1-one (6b):** a

yellow solid; mp 128–130 °C (hexane/ $CH_2Cl_2$ ); IR (KBr) 3226, 1638  $cm^{-1}$ ;  $^1H$  NMR  $\delta$  2.56 (s, 3H), 3.10 (d,  $J = 4.6$  Hz, 3H), 4.07 (s, 3H), 7.26 (t,  $J = 7.4$  Hz, 1H), 7.39 (t,  $J = 7.4$  Hz, 2H), 7.41 (br, 1H), 7.58 (d,  $J = 7.4$  Hz, 2H), 7.63 (d,  $J = 14.9$  Hz, 1H), 7.75 (d,  $J = 14.9$  Hz, 1H). HR-MS (EI). Calcd for  $C_{16}H_{17}N_3O_2S$  (M): 315.1041. Found:  $m/z$  315.1045. Anal. Calcd for  $C_{16}H_{17}N_3O_2S$ : C, 60.93; H, 5.43; N, 13.32. Found: C, 60.83; H, 5.41; N, 13.31.

**7-(4-Chlorophenyl)-4-methoxy-8-methyl-2-(methylsulfanyl)-6,7-dihydropyrido[2.3-*d*]pyridin-5(8*H*)-one (5c).** This compound was obtained accompanying **6c**. A pale-yellow solid; mp 166–168 °C

(hexane/ $CH_2Cl_2$ ); IR (KBr) 1674  $cm^{-1}$ ;  $^1H$  NMR  $\delta$  2.56 (s, 3H), 2.73 (dd,  $J = 15.5, 3.4$  Hz, 1H), 3.17 (dd,  $J = 15.5, 6.9$  Hz, 1H), 3.20 (s, 3H), 4.03 (s, 3H), 4.70 (dd,  $J = 6.9, 3.4$  Hz, 1H), 7.05 (d,  $J = 8.0$  Hz, 2H), 7.28 (d,  $J = 8.0$  Hz, 2H);  $^{13}C$  NMR  $\delta$  14.20, 35.96, 44.53, 54.63, 60.94, 94.89, 127.45, 129.31, 134.04, 136.84, 163.09, 166.68, 175.80, 187.75. HR-MS (EI). Calcd for  $C_{16}H_{16}ClN_3O_2S_2$  (M): 349.0652. Found:  $m/z$  349.0668. Anal. Calcd for  $C_{16}H_{16}ClN_3O_2S_2$ : C, 54.93; H, 4.61; N, 12.01. Found: C, 54.96; H, 4.63; N, 11.97.

**3-(4-Chlorophenyl)-1-[3-methoxy-5-(methylamino)-2-(methylsulfanyl)]pyrimidin-4-yl]prop-2-en-1-**

**one (6c):** a pale-yellow solid; mp 124–126 °C (hexane/ $CH_2Cl_2$ ); IR (KBr) 3194, 1638  $cm^{-1}$ ;  $^1H$  NMR  $\delta$  2.55 (s, 3H), 3.09 (d,  $J = 4.6$  Hz, 3H), 4.06 (s, 3H), 7.36 (d,  $J = 8.6$  Hz, 2H), 7.50 (d,  $J = 8.6$  Hz, 2H), 7.56 (d,  $J = 15.5$  Hz, 1H), 7.70 (d,  $J = 15.5$  Hz, 1H), 9.86 (br s, 1H). HR-MS (EI). Calcd for  $C_{16}H_{16}ClN_3O_2S_2$  (M): 349.0652. Found:  $m/z$  349.0660. Anal. Calcd for  $C_{16}H_{16}ClN_3O_2S_2$ : C, 54.93; H, 4.61; N, 12.01. Found: C, 54.96; H, 4.63; N, 11.97.

**4-Methoxy-7-(4-methoxyphenyl)-2-(methylsulfanyl)-8-(2-phenylethyl)-6,7-dihydropyrido[2.3-*d*]pyridin-5(8*H*)-one (5d).** This compound was obtained accompanying **6d**. A white solid; mp 152–154

°C (hexane/ $CH_2Cl_2$ ); IR (KBr) 1677, 1636  $cm^{-1}$ ;  $^1H$  NMR  $\delta$  2.57–2.61 (m, including s at 2.59, combined 4H), 2.85–2.94 (m, 2H), 3.02–3.05 (m, 1H), 3.11–3.15 (m, 1H), 3.75 (s, 3H), 4.04 (s, 3H), 4.33–4.35 (m, 1H), 4.47–4.52 (m, 2H), 6.78 (d,  $J = 8.4$  Hz, 2H), 6.95 (d,  $J = 8.4$  Hz, 1H), 7.16–7.31 (m, 5H);  $^{13}C$  NMR

$\delta$  14.26, 34.35, 44.54, 50.38, 54.63, 55.26, 59.62, 94.77, 114.32, 126.61, 127.30, 128.58, 128.82, 130.24, 138.89, 159.31, 162.52, 166.66, 175.46, 188.39. HR-MS (ESI, positive). Calcd for  $C_{24}H_{26}N_3O_3S$  (M+H): 436.1695. Found:  $m/z$  436.1682. Anal. Calcd for  $C_{24}H_{25}N_3O_3S$ : C, 66.18; H, 5.79; N, 9.65; S, 7.36. Found: C, 66.25; H, 5.60; N, 9.30; S, 7.42.

**1-[3-Methoxy-2-(methylsulfanyl)-5-[(2-phenylethyl)amino]pyrimidin-4-yl]-3-(4-methoxyphenyl)prop-2-en-1-one (6d)**: a yellow solid; mp 106–108 °C (hexane/ $CH_2Cl_2$ ); IR (neat) 3227, 1634  $cm^{-1}$ ;  $^1H$  NMR  $\delta$  2.56 (s, 3H), 2.95 (t,  $J = 7.6$  Hz, 2H), 3.79 (q,  $J = 7.6$  Hz, 2H), 3.85 (s, 3H), 4.06 (s, 3H), 6.92 (d,  $J = 8.4$  Hz, 2H), 7.21–7.26 (m, 3H), 7.32 (dd,  $J = 7.6, 6.9$  Hz, 2H), 7.54 (d,  $J = 8.4$  Hz, 2H), 7.62 (s, 2H), 10.05 (br s, 1H);  $^{13}C$  NMR  $\delta$  14.18, 35.89, 42.83, 54.27, 55.33, 95.40, 114.22, 125.72, 126.36, 128.27, 128.51, 128.73, 129.81, 139.16, 140.67, 161.01, 162.64, 168.29, 173.59, 189.37. HR-MS (ESI). Calcd for  $C_{24}H_{26}N_3O_3S$  (M+H): 436.1695. Found:  $m/z$  436.1684. Anal. Calcd for  $C_{24}H_{25}N_3O_3S$ : C, 66.18; H, 5.79; N, 9.65; S, 7.36. Found: C, 66.02; H, 5.56; N, 9.63; S, 7.64.

**4-Methoxy-7-(4-methoxyphenyl)-8-methyl-2-(methylsulfanyl)-6,7-dihydropyrido[2.3-*d*]pyridin-5(8*H*)-one (5e)**. This compound was obtained accompanying **6e**. A white solid; mp 120–122 °C (hexane/ $CH_2Cl_2$ ); IR (KBr) 1674, 1611  $cm^{-1}$ ;  $^1H$  NMR  $\delta$  2.56 (s, 3H), 2.75 (dd,  $J = 15.3, 3.8$  Hz, 1H), 3.14 (dd,  $J = 15.3, 6.9$  Hz, 1H), 3.19 (s, 3H), 3.77 (s, 3H), 4.03 (s, 3H), 4.67 (dd,  $J = 6.9, 3.8$  Hz, 1H), 6.82 (d,  $J = 8.4$  Hz, 2H), 7.04 (d,  $J = 8.4$  Hz, 2H);  $^{13}C$  NMR  $\delta$  14.20, 35.82, 44.86, 54.60, 55.27, 60.96, 94.81, 114.41, 127.28, 130.26, 159.34, 163.05, 166.66, 175.47, 188.49. HR-MS (EI). Calcd for  $C_{17}H_{19}N_3O_3S$  (M): 345.1147. Found:  $m/z$  345.1143. Anal. Calcd for  $C_{17}H_{19}N_3O_3S$ : C, 59.11; H, 5.54; N, 12.17; S, 9.28. Found: C, 58.95; H, 5.26; N, 12.29; S, 9.39.

**1-[3-Methoxy-5-(methylamino)-2-(methylsulfanyl)]pyrimidin-4-yl]-3-(4-methoxyphenyl)prop-2-en-1-one (6e)**: a yellow solid; mp 137–139 °C (hexane/ $CH_2Cl_2$ ); IR (KBr) 3237, 1634  $cm^{-1}$ ;  $^1H$  NMR  $\delta$  2.55 (s, 3H), 3.08 (d,  $J = 5.4$  Hz, 3H), 3.84 (s, 3H), 4.06 (s, 3H), 6.92 (d,  $J = 8.4$  Hz, 2H), 7.53 (d,  $J = 8.4$  Hz, 2H), 7.61 (d,  $J = 16.1$  Hz, 1H), 7.65 (d,  $J = 16.1$  Hz, 1H), 9.86 (br s, 1H). HR-MS (EI). Calcd for  $C_{17}H_{19}N_3O_3S$  (M): 345.1147. Found:  $m/z$  345.1151. Anal. Calcd for  $C_{17}H_{19}N_3O_3S$ : C, 59.11; H, 5.54; N, 12.17; S, 9.28. Found: C, 58.98; H, 5.25; N, 12.22; S, 9.34.

**Typical Procedure for the Preparation of Pyridopyrimidinones 7. 2-[4-Methoxy-7-methyl-2-(methylsulfanyl)-5-oxo-5,6,7,8-tetrahydropyrido[2.3-*d*]pyridin-8-yl]acetonitrile (7a)**. A solution of **2a** (0.13 g, 0.50 mmol) and  $NCCH_2NH_3^+Cl^-$  (46 mg, 0.50 mmol) in DMF (3 mL) containing  $Et_3N$  (0.10 g, 1.0 mmol) was stirred at room temperature for 7 h. The mixture was worked up as described for the preparation of **4a** and the crude product was purified by recrystallization from hexane/ $CH_2Cl_2$  to afford **7a** (0.10 g, 74%); a white solid; mp 137–139 °C; IR (KBr) 2249, 1685  $cm^{-1}$ ;  $^1H$  NMR  $\delta$  1.35 (d,  $J = 6.9$  Hz, 3H), 2.50 (dd,  $J = 16.0, 3.8$  Hz, 1H), 2.57 (s, 3H), 2.97 (dd,  $J = 16.0, 6.1$  Hz, 1H), 3.95–3.99 (m, 1H), 4.07 (s, 3H), 4.45 (d,  $J = 16.8$  Hz, 1H), 5.74 (d,  $J = 16.8$  Hz, 1H);  $^{13}C$  NMR  $\delta$  14.24, 16.45, 35.27, 44.31,

53.12, 54.97, 95.10, 115.64, 161.19, 166.78, 176.11, 188.33. HR-MS (ESI). Calcd for  $C_{12}H_{15}N_4O_2S$  (M+H): 279.0915. Found:  $m/z$  279.0910. Anal. Calcd for  $C_{12}H_{14}N_3O_2S$ : C, 51.78; H, 5.07; N, 20.13. Found: C, 51.40; H, 5.07; N, 19.75.

**Ethyl 2-[4-Methoxy-7-methyl-2-(methylsulfonyl)-5-oxo-5,6,7,8-tetrahydropyrido[2.3-*d*]pyridin-8-yl]acetate (7b)**: a white solid; mp 137–139 °C (hexane/ $CH_2Cl_2$ ); IR (KBr) 1749, 1668  $cm^{-1}$ ;  $^1H$  NMR  $\delta$  1.25 (d,  $J = 6.1$  Hz, 3H), 1.29 (t,  $J = 7.6$  Hz, 3H), 2.45 (dd,  $J = 15.3, 3.1$  Hz, 1H), 2.46 (s, 3H), 3.02 (dd,  $J = 15.3, 6.1$  Hz, 1H), 3.80–3.86 (m, 1H), 3.97 (d,  $J = 17.6$  Hz, 1H), 4.04 (s, 3H), 4.22 (q,  $J = 7.6$  Hz, 2H), 4.78 (d,  $J = 17.6$  Hz, 1H);  $^{13}C$  NMR  $\delta$  14.03, 14.18, 16.81, 43.95, 49.01, 52.73, 54.70, 61.34, 94.29, 161.58, 166.69, 169.39, 175.30, 189.27. HR-MS (EI). Calcd for  $C_{14}H_{19}N_3O_4S$ : 325.1096. Found:  $m/z$  325.1100. Anal. Calcd for  $C_{14}H_{19}N_3O_4S$ : C, 51.68; H, 5.89; N, 12.91. Found: C, 51.73; H, 5.67; N, 13.17.

**2-[7-Ethyl-4-methoxy-2-(methylsulfonyl)-5-oxo-5,6,7,8-tetrahydropyrido[2.3-*d*]pyridin-8-yl]acetonitrile (7c)**: a yellow solid; mp 183–185 °C (hexane/ $CH_2Cl_2$ ); IR (KBr) 2350, 1677  $cm^{-1}$ ;  $^1H$  NMR  $\delta$  0.96 (t,  $J = 7.4$  Hz, 3H), 1.66–1.73 (m, 1H), 1.77–1.82 (m, 1H), 2.57 (s, 3H), 2.65 (dd,  $J = 16.0, 2.9$  Hz, 1H), 2.92 (dd,  $J = 16.0, 6.3$  Hz, 1H), 3.69–3.70 (m, 1H), 4.06 (s, 3H), 4.37 (d,  $J = 17.2$  Hz, 1H), 4.81 (d,  $J = 17.2$  Hz, 1H);  $^{13}C$  NMR  $\delta$  9.87, 14.24, 23.39, 35.96, 40.85, 54.92, 58.83, 95.21, 115.62, 161.37, 166.70, 176.08, 188.28. HR-MS (EI). Calcd for  $C_{13}H_{16}N_4O_2S$ : 292.0994. Found:  $m/z$  292.1005. Anal. Calcd for  $C_{13}H_{16}N_4O_2S$ : C, 53.41; H, 5.52; N, 19.16. Found: C, 53.34; H, 5.60; N, 19.17.

**8-(3-Bromopropyl)-4-methoxy-7-methyl-2-(methylsulfonyl)-6,7-dihydropyrido[2.3-*d*]pyridin-5(8*H*)-one (8)**. A solution of **2a** (0.13 g, 0.50 mmol) and  $Br(CH_2)_3NH_3^+Br^-$  (0.11 g, 0.50 mmol) in DMF (4 mL) containing  $Et_3N$  (0.10 g, 1.0 mmol) was stirred at 0 °C for 30 min. The mixture was worked up as described for the preparation of **4a** and the crude product was purified by column chromatography on  $SiO_2$  (AcOEt/hexane 2:1) to afford **8** (44 mg, 25%); a white solid; mp 144–146 °C (hexane/ $CH_2Cl_2$ ); IR (KBr) 1686  $cm^{-1}$ ;  $^1H$  NMR  $\delta$  1.36 (d,  $J = 6.9$  Hz, 3H), 2.32–2.36 (m, 1H), 2.47 (dd,  $J = 16.1, 2.3$  Hz, 1H), 2.56–2.63 (m, 1H), 2.73 (s, 3H), 3.50 (dd,  $J = 16.1, 6.9$  Hz, 1H), 3.88–3.92 (m, 1H), 4.09–4.15 (m, 1H), 4.19 (s, 3H), 4.22–4.27 (m, 1H), 4.40–4.45 (m, 1H), 4.53–4.58 (m, 1H);  $^{13}C$  NMR  $\delta$  16.13, 16.36, 18.92, 42.32, 45.91, 46.57, 56.18, 56.54, 93.54, 153.64, 163.42, 170.28, 186.78. HR-MS (DART). Calcd for  $C_{13}H_{17}N_3O_2S$  [(M–HBr)+H]: 280.1118. Found:  $m/z$  280.1118. Anal. Calcd for  $C_{13}H_{18}BrN_3O_2S$ : C, 43.34; H, 5.04; N, 11.66. Found: C, 43.57; H, 5.12; N, 11.64.

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