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SYNTHESIS OF 7,8-DIHYDROPYRIDO[2,3-*d*]PYRIMIDINE DERIVATIVES FROM 4,6-DICHLORO-2-(METHYLSULFANYL)PYRIMIDINE

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Abstract – A new and convenient method for the preparation of 7,8-dihydropyrido[2,3-*d*]pyrimidine derivatives has been developed utilizing a three-step sequence starting with a commercially available 4,6-dichloro-2-(methylsulfanyl)pyrimidine (DCSMP). Thus, successive treatment of the starting material with LDA and cinnamaldehyde or its derivatives leads to the formation of 3-aryl-1-[4,6-dichloro-2-(methylsulfanyl)pyrimidin-5-yl]prop-2-en-1-ols. After replacement of one of the two chloro-substituents with primary amines, cyclization of the resulting precursors gives the desired products on treatment with methanesulfonyl chloride in the presence of triethylamine.

INTRODUCTION

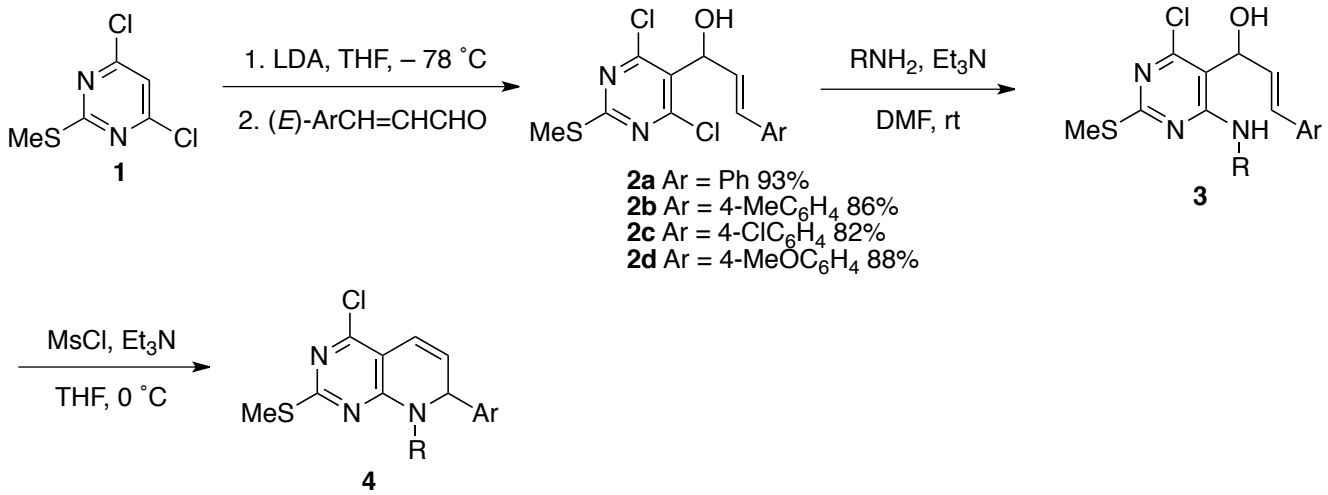
A number of 7,8-dihydropyrido[2,3-*d*]pyrimidine derivatives have recently been synthesized, and most of them have been shown to exhibit a wide variety of biological activities.[1] Therefore, some methods for the general preparation of these derivatives has been developed.[2] Liu *et al*. have reported the synthesis by the reaction of α-alkenoyl-α-carbamoyl ketene-*S*,*S*-acetals with ammonium acetate followed by annulation with excessive Vilsmeier reagent.[2a] The synthesis by three-component condensation of 5-acetyl-4-aminopyrimidines, cyclohexane-1,3-diones, and orthocarboxylic acid esters has been reported by Dorokhov *et al*.[2b] These methods, however, have defects such as limited scope and somewhat harsh

reaction conditions. In a continuation of our studies on the syntheses of pyrimidine-fused heterocyclic derivatives utilizing 4,6-dichloro-2-(methylsulfanyl)pyrimidine (DCSMP) (**1**) as a starting material,[3] we now wish to report an efficient three-step procedure for the preparation of a new type of 7,8-dihydropyrido[2,3-*d*]pyrimidine derivatives, 8-alkyl-7-aryl-4-chloro-2-(methylsulfanyl)-7,8-dihydropyrido[2,3-*d*]pyrimidines (**4**) from **1**, which can be conducted under mild conditions.

RESULTS AND DISCUSSION

Our three-step synthesis of **4** from commercially available **1** was conducted according to the sequence outlined in Scheme 1. Thus, the starting material (**1**) was lithiated at the 5-position with LDA in THF at –78 ˚C to generate 4,6-dichloro-5-lithio-2-(methylsulfanyl)pyrimidine,[3a] which was allowed to react with cinnamaldehyde and its derivatives to give the corresponding 3-aryl-1-[4,6-dichloro-2-(methylsulfanyl)pyrimidin-5-yl]prop-2-en-1-ols (**2**) in good yields, as shown in Scheme 1. Replacement of one of the two chloro-substituents of **2** with primary amines proceeded relative smoothly and cleanly in DMF at room temperature in the presence of triethylamine to provide 1-[4-(alkylamino)-6-chloro-2-(methylsulfanyl)pyrimidin-5-yl]-3-arylprop-2-en-1-ols (**3**) in generally good to excellent yields, as summarized in Table 1.

Subsequent cyclization of compounds **3**, thus obtained, using an equivalent each of methanesulfonyl chloride and triethylamine in THF proceeded quickly at 0 ˚C. After aqueous workup and the subsequent purification by column chromatography on silica gel or recrystallization, the desired 7,8-dihydropyrido[2,3-*d*]pyrimidine derivatives (**4**) were obtained, albeit in generally moderate yields, as compiled in Table 1 as well.



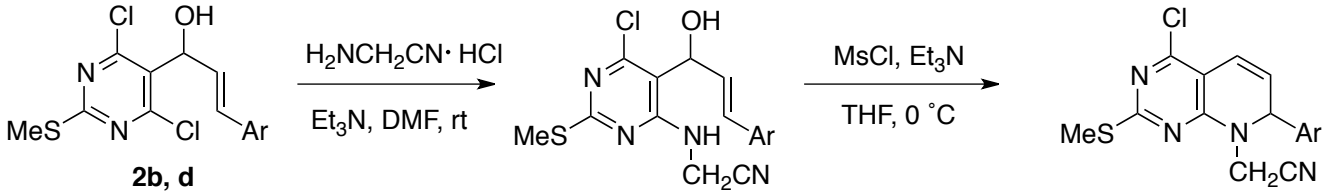
Scheme 1

Table 1. Preparation of 7,8-dihydropyrido[2,3-*d*]pyrimidines (**4**)

Entry	**2**	R in RNH_2	**3**	Yield/%[a]	**4**	Yield/%[a]
1	**2a** (Ar = Ph)	*n*-Bu	**3a**	79	**4a**	64
2	**2a**	Bn	**3b**	84	**4b**	52
3	**2a**	$MeO(CH_2)_2$	**3c**	74	**4c**	85
4	**2b** (Ar = 4-MeC_6H_4)	Me	**3d**	93	**4d**	51
5	**2b**	3,4-$Cl_2C_6H_3CH_2$	**3e**	91	**4e**	48
6	**2c** (Ar = 4-ClC_6H_4)	Me	**3f**	93	**4f**	43
7	**2c**	$Ph(CH_2)_2$	**3g**	91	**4g**	45
8	**2d** (Ar = 4-$MeOC_6H_4$)	Me	**3h**	72	**4h**	66
9	**2d**	Bn	**3i**	61	**4i**	52
10	**2d**	4-$ClC_6H_4CH_2$	**3j**	53	**4j**	59
11	**2d**	cyclopropyl	**3k**	69	**4k**	54

[a] Yields of isolated products.

In order to expand the synthetic potential of the present methodology, attempts at the use of 2-aminoacetonitrile as a primary amine were carried out. Thus, compounds (**2b**) and (**2d**) were allowed to react with 2-aminoacetonitrile hydrochloride in DMF in the presence of two equivalents of triethylamine at room temperature. We have found that this amine was much less reactive than the other primary amines used in this study, and the reactions proceeded very slowly to give (cyanomethyl)amino products (**5b**) and (**5d**), respectively, only in moderate yields. However, transformation of these compounds into the corresponding 7,8-dihydropyrido[2,3-*d*]pyrimidine derivatives (**6b**) and (**6d**) proceeded very cleanly and rapidly with high yields under the same conditions as described for the preparation of **4**, as shown in Scheme 2.



Scheme 2

It is noteworthy that an attempt to obtain 7,8-dimethyl-7,8-dihydropyrimido[2,3-*d*]pyrimidine from the respective precursor, prepared similarly from DCSMP, crotonaldehyde and methylamine, under the same conditions as described above was unsuccessful. The reaction gave an intractable mixture of products. The expected product may be too unstable to survive under the reaction conditions.

In conclusion, we have developed a convenient method for the preparation of 8-alkyl-7-aryl-7,8-dihydropyrido[2,3-*d*]pyrimidine derivatives. The present method may be of value in organic synthesis because of the ease of operations, as well as the ready availability of the starting materials, and it may

offer the possibility to access compounds of potential biological importance through further functionalization at the 2- and 4-positions.

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 Spectrum 65 FTIR spectrophotometer. ^{11}H NMR and ^{13}C NMR spectra were recorded using TMS as an internal reference with a Bruker Biospin AVANCE II 600 spectrometer operating at 600 MHz and 150 MHz, respectively, or a JEOL ECP500 FT NMR spectrometer operating at 500 and 125 MHz, respectively. High-resolution MS spectra were measured by a Thermo Scientific Exactive spectrometer (ESI, positive) or a JEOL JMS-T100GCV (EI, TOF; 70 eV) spectrometer. Elemental analyses were performed with an Elementar Vario EL II instrument. TLC was carried out on Merck Kieselgel 60 PF_{254}. 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. *n*-BuLi was supplied by Asia Lithium Corporation. All other chemicals used in this study were commercially available.

Typical Procedure for the Preparation of 3-Aryl-1-[4,6-dichloro-2-(methylsulfanyl)pyrimidin-5-yl]prop-2-en-1-ols (2). 1-[4,6-Dichloro-2-(methylsulfanyl)pyrimidin-5-yl]-3-phenylprop-2-en-1-ol (2a). To a stirred solution of LDA (10 mmol), generated from *i*-Pr_2NH and *n*-BuLi by the standard method, in THF (15 mL) at –78 ˚C was added a solution of **1** (0.97 g, 5.0 mmol) in THF (5 mL) dropwise. After 30 min, (*E*)-PhCH=CHCHO (0.66 g, 5.0 mmol) was added and stirring was continued for an additional 10 min before addition of saturated aqueous NH_4Cl (30 mL). The mixture was warmed to rt and extracted with AcOEt (3 × 20 mL). The combined extracts were washed with brine (20 mL), dried (Na_2SO_4), and concentrated by evaporation. The residue was purified by column chromatography on SiO_2 to give **2a** (1.5 g, 93%); a pale-yellow oil; R_f 0.25 (AcOEt/hexane 1:6); IR (neat) 3438, 1646 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.58 (s, 3H), 2.77 (d, *J* = 9.2 Hz, 1H), 5.97 (dd, *J* = 9.2, 6.3 Hz, 1H), 6.50 (dd, *J* = 16.0, 6.3 Hz, 1H), 6.67 (d, *J* = 16.0 Hz, 1H), 7.27 (t, *J* = 7.4 Hz, 1H), 7.33 (t, *J* = 7.4 Hz, 2H), 7.39 (d, *J* = 7.4 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.41, 70.46, 125.80, 126.40, 126.68, 128.30, 128.66, 132.67, 135.78, 160.37, 172.12. Anal. Calcd for $C_{14}H_{12}Cl_2N_2OS$: C, 51.39; H, 3.70; N, 8.56. Found: C, 51.40; H, 3.79; N, 8.42.

1-[4,6-Dichloro-2-(methylsulfanyl)pyrimidin-5-yl]-3-(4-methylphenyl)prop-2-en-1-ol (2b): a white solid; mp 108–111 ˚C (hexane/CH_2Cl_2); IR (KBr) 3413, 1646, 1611 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.34 (s, 3H), 2.57 (s, 3H), 2.75 (d, *J* = 8.4 Hz, 1H), 5.94–5.96 (m, 1H), 6.45 (dd, *J* = 16.2, 6.0 Hz, 1H), 6.63 (dd, *J* = 16.2, 1.2 Hz, 1H), 7.13 (d, *J* = 7.8 Hz, 2H), 7.28 (d, *J* = 7.8 Hz, 2H); ^{13}C NMR (150 MHz,

$CDCl_3$) δ 14.44, 21.25, 70.67, 125.33, 125.94, 126.66, 129.41, 132.79, 133.04, 138.36, 160.40, 172.10. Anal. Calcd for $C_{15}H_{14}Cl_2N_2OS$: C, 52.80; H, 4.14; N, 8.21. Found: C, 52.87; H, 4.22; N, 8.05.

3-(4-Chlorophenyl)-1-[4,6-dichloro-2-(methylsulfanyl)pyrimidin-5-yl]prop-2-en-1-ol (2c): a white solid; mp 132–135 ˚C (hexane/CH_2Cl_2); IR (KBr) 3415 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.50 (s, 3H), 2.75 (d, *J* = 8.0 Hz, 1H), 5.89 (dd, *J* = 8.0, 6.3 Hz, 1H), 6.40 (dd, *J* = 15.5, 6.3 Hz, 1H), 6.56 (d, *J* = 15.5 Hz, 1H), 7.22 (d, *J* = 9.2 Hz, 2H), 7.23 (d, *J* = 9.2 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.42, 70.33, 125.57, 127.09, 127.89, 128.85, 131.38, 133.99, 134.28, 160.35, 172.30. Anal. Calcd for $C_{14}H_{11}Cl_3N_2OS$: C, 46.49; H, 3.07; N, 7.75. Found: C, 46.62; H, 3.17; N, 7.73.

1-[4,6-Dichloro-2-(methylsulfanyl)pyrimidin-5-yl]-3-(4-methoxyphenyl)prop-2-en-1-ol (2d): a pale-yellow oil; R_f 0.30 (AcOEt/hexane 1:3); IR (neat) 3411, 1607 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.57 (s, 3H), 2.77 (d, *J* = 8.6 Hz, 1H), 3.81 (s, 3H), 5.94 (ddd, *J* = 8.6, 6.3, 1.7 Hz, 1H), 6.39 (ddd, *J* = 16.0, 8.6, 1.7 Hz, 1H), 6.61 (d, *J* = 16.0 Hz, 1H), 6.86 (d, *J* = 8.6 Hz, 2H), 7.32 (d, *J* = 8.6 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.40, 55.29, 70.72, 114.08, 124.00, 125.97, 127.98, 128.51, 132.45, 159.76, 160.33, 171.99. MR-MS (EI). Calcd for $C_{15}H_{14}Cl_2N_2O_2S$ (M): 356.0153. Found: *m/z* 356.0153.

Typical Procedure for the Preparation of 1-[4-(Alkylamino)pyrimidin-5-yl]-3-phenylprop-2-en-1-ols (3). 1-[4-Butylamino-6-chloro-2-(methylsulfanyl)pyrimidin-5-yl]-3-phenylprop-2-en-1-ol (3a). To a stirred solution of **2a** (0.44 g, 1.3 mmol) in DMF (3 mL) containing Et_3N (0.14 g, 1.3 mmol) at 0 ˚C was added *n*-$BuNH_2$ (98 mg, 1.3 mmol) dropwise and stirring was continued for 1.5 h at the same temperature. Water (20 mL) was added and the mixture was extracted with AcOEt (3 × 10 mL). The combined extracts were washed with H_2O (3 × 10 mL) and brine (10 mL), dried (Na_2SO_4), and concentrated by evaporation. The residue was purified by column chromatography on SiO_2 to afford **3a** (0.39 g, 79%); a yellow oil; R_f 0.20 (CH_2Cl_2); IR (neat) 3367, 1644, 1567 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.88 (t, *J* = 7.6 Hz, 3H), 1.32–1.36 (m, 2H), 1.52–1.57 (m, 2H), 2.50 (s, 3H), 2.65 (d, *J* = 2.3 Hz, 1H), 3.40–3.44 (m, 1H), 3.50–3.53 (m, 1H), 5.96 (br s, 1H), 6.30 (dd, *J* = 15.3, 4.6 Hz, 1H), 6.67–6,70 (m, 2H), 7.25 (t, *J* = 7.6 Hz, 1H), 7.32 (t, *J* = 7.6 Hz, 2H), 7.37 (d, *J* = 7.6 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.72, 14.07, 20.11, 31.21, 40.82, 70.32, 108.29, 126.25, 126.59, 127.93, 128.56, 131.00, 136.15, 155.15, 160.59, 170.28. MR–MS (EI). Calcd for $C_{18}H_{22}ClN_3OS$ (M): 363.1172. Found: *m/z* 363.1158.

1-{6-Chloro-2-(methylsulfanyl)-4-[(phenylmethyl)amino]pyrimidin-5-yl}-3-phenylprop-2-en-1-ol (3b): colorless needles; mp 125–127 ˚C (hexane/CH_2Cl_2); IR (KBr) 3382, 3279, 1659, 1574 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.44 (s, 3H), 3.08 (br s, 1H), 4.57 (dd, *J* = 15.3, 4.6 Hz, 1H), 4.78 (dd, *J* = 15.3, 6.1 Hz, 1H), 5.96–5.97 (m, 1H), 6.31 (dd, *J* = 16.1, 5.4 Hz, 1H), 6.66 (dd, *J* = 16.1, 1.5 Hz, 1H), 7.11 (br t, *J* = 5.4 Hz, 1H), 7.21–7.27 (m, 6H), 7.30–7.34 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.08, 44.91, 70.21, 108.64, 126.44, 126.62, 127.15, 127.29, 127.92, 128.53, 128.55, 130.88, 136.10, 138.47,

155.38, 160.53, 170.35. Anal. Calcd for $C_{21}H_{20}ClN_3OS$: C, 63.39; H, 5.07; N, 10.56. Found: C, 63.12; H, 4.99; N, 10.49.

1-{6-Chloro-4-[(2-methoxyethyl)amino]-2-(methylsulfanyl)pyrimidin-5-yl}-3-phenylprop-2-en-1-ol (3c): a white solid; mp 100–102 °C (hexane/CH_2Cl_2); IR (KBr) 3324, 3236, 1583 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.49 (s, 3H), 2.58 (br s, 1H), 3.29 (s, 3H), 3.45–3.49 (m, 1H), 3.53–3.57 (m, 1H), 3.60–3.66 (m, 1H), 3.68–3.74 (m, 1H), 5.96 (d, *J* = 5.3 Hz, 1H), 6.33 (dd, *J* = 16.0, 5.3 Hz, 1H), 6.72 (d, *J* = 16.0 Hz, 1H), 6.98 (br s, 1H), 7.25 (t, *J* = 7.6 Hz, 1H), 7.31 (t, *J* = 7.6 Hz, 2H), 7.37 (d, *J* = 7.6 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.11, 40.72, 58.76, 70.47, 70.81, 108.53, 126.16, 126.62, 127.94, 128.56, 131.10, 136.16, 155.48, 160.51, 170.33. Anal. Calcd for $C_{17}H_{20}ClN_3O_2S$: C, 55.81; H, 5.51; N, 11.49. Found: C, 55.81; H, 5.46; N, 11.41.

1-{6-Chloro-4-(methylamino)-2-(methylsulfanyl)pyrimidin-5-yl}-3-(4-methylphenyl)prop-2-en-1-ol (3d): a white solid; mp 152–154 °C (hexane/CH_2Cl_2); IR (KBr) 3379, 1568 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 2.32 (s, 3H), 2.51 (s, 3H), 2.99 (d, *J* = 5.0 Hz, 3H), 3.19 (s, 1H), 5.90 (d, *J* = 5.5 Hz, 1H), 6.24 (dd, *J* = 16.0, 5.0 Hz, 1H), 6.62 (dd, *J* =16.0, 1.0 Hz, 1H), 6.76 (q, *J* = 5.0 Hz, 1H), 7.11 (d, *J* = 8.0 Hz, 2H), 7.26 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 14.11, 21.23, 28.13, 70.70, 108.70, 125.03, 126.60, 129.32, 131.26, 133.33, 137.99, 155.14, 161.18, 170.33. Anal. Calcd for $C_{16}H_{18}ClN_3OS$: C, 57.22; H, 5.40; N, 12.51. Found: C, 56.99; H, 5.35; N, 12.21.

1-{6-Chloro-4-{[(3,4-dichlorophenyl)methyl]amino}-2-(methylsulfanyl)pyrimidin-5-yl}-3-(4-methylphenyl)prop-2-en-1-ol (3e): a white solid; mp 123–126 °C (hexane/CH_2Cl_2); IR (KBr) 3356, 1578 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 2.34 (s, 3H), 2.42 (s, 3H), 3.09 (d, *J* = 2.0 Hz, 1H), 4.52 (dd, *J* = 15.4, 5.9 Hz, 1H), 4.73 (dd, *J* = 15.4, 5.9 Hz, 1H), 5.95 (dd, *J* = 5.2, 1.1 Hz, 1H), 6.25 (dd, *J* = 16.0, 5.2 Hz, 1H), 6.62 (dd, *J* = 16.0, 1.1 Hz, 1H), 7.06 (dd, *J* = 8.2, 2.0 Hz, 1H), 7.13 (d, *J* = 8.0 Hz, 2H), 7.15 (t, *J* = 5.9 Hz, 1H), 7.24 (d, *J* = 8.0 Hz, 2H), 7.25 (d, *J* = 8.2 Hz, 1H), 7.34 (d, *J* = 2.0 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 14.13, 21.25, 43.85, 70.50, 108.81, 124.90, 126.59, 126.65, 129.26, 129.40, 130.54, 131.17, 131.27, 132.59, 133.59, 138.17, 139.01, 155.72, 160.47, 170.59. Anal. Calcd for $C_{22}H_{20}Cl_3N_3OS$: C, 54.96; H, 4.19; N, 8.74. Found: C, 55.13; H, 4.26; N, 8.73.

1-{6-Chloro-4-(methylamino)-2-(methylsulfanyl)pyrimidin-5-yl}-3-(4-chlorophenyl)prop-2-en-1-ol (3f): a white solid; mp 193–196 °C (hexane/CH_2Cl_2); IR (KBr) 3392, 1569 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6) δ 2.47 (s, 3H), 2.94 (d, *J* = 4.6 Hz, 3H), 5.71 (br s, 1H), 6.42–6.45 (m, 2H), 6.70 (d, *J* = 16.1 Hz, 1H), 7.30 (br s, 1H), 7.39 (d, *J* = 8.6 Hz, 2H), 7.51 (d, *J* = 8.6 Hz, 2H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 13.45, 28.00, 68.88, 109.54, 128.26, 128.36, 128.61, 128.86, 132.08, 135.20, 153.90, 160.65, 168.76. Anal. Calcd for $C_{15}H_{15}Cl_2N_3OS$: C, 50.57; H, 4.24; N, 11.79. Found: C, 50.39; H, 4.26; N, 11.83.

1-{6-Chloro-2-(methylsulfanyl)-4-[(2-phenylethyl)amino]pyrimidin-5-yl}-3-(4-chlorophenyl)prop-2-en-1-ol (3g): a white solid; mp 130–133 °C (hexane/CH_2Cl_2); IR (KBr) 3360, 1568 cm^{-1}; ^1H NMR (500

MHz, $CDCl_3$) δ 2.51 (s, 3H), 2.84–2.93 (m, 2H), 3.65–3.71 (m, 1H), 3.75–3.80 (m, 1H), 5.85 (dd, *J* = 5.7, 1.1 Hz, 1H), 6.13 (dd, *J* = 16.0, 5.7 Hz, 1H), 6.52 (d, *J* = 16.0 Hz, 1H), 6.82 (t, *J* = 5.7 Hz, 1H), 7.16–7.18 (m, 10H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.14, 35.23, 42.46, 70.45, 108.21, 126.48, 126.61, 127.88, 128.55, 128.70, 128.75, 129.99, 133.64, 134.54, 138.89, 155.26, 160.43, 170.43. Anal. Calcd for $C_{22}H_{21}Cl_2N_3OS$: C, 59.20; H, 4.74; N, 9.41. Found: C, 59.06; H, 4.89; N, 9.03.

1-{6-Chloro-4-(methylamino)-2-(methylsulfanyl)pyrimidin-5-yl}-3-(4-methoxyphenyl)prop-2-en-1-ol (3h): a yellow solid; mp 142–144 °C (hexane/CH_2Cl_2); IR (KBr) 3400, 3309, 1605, 1575 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.51 (s, 3H), 2.99 (d, *J* = 5.2 Hz, 3H), 3.30 (br, 1H), 3.80 (s, 3H), 5.89 (d, *J* = 4.6 Hz, 1H), 6.16 (dd, *J* = 15.4, 5.7 Hz, 1H), 6.59 (d, *J* = 15.4 Hz, 1H), 6.77 (d, *J* = 4.6 Hz, 1H), 6.84 (d, *J* = 9.2 Hz, 2H), 7.30 (d, *J* = 9.2 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.07, 28.09, 55.29, 70.78, 108.73, 113.99, 123.80, 127.90, 128.82, 130.90, 155.08, 159.52, 161.16, 170.25. Anal. Calcd for $C_{16}H_{18}ClN_3O_2S$: C, 54.62; H, 5.16; N, 11.94. Found: C, 54.45; H, 5.38; N, 11.92.

1-{6-Chloro-2-(methylsulfanyl)-4-[(phenylmethyl)amino]pyrimidin-5-yl}-3-(4-methoxyphenyl)prop-2-en-1-ol (3i): a white solid; mp 118–120 °C (hexane/CH_2Cl_2); IR (KBr) 3426, 3350, 1607 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.44 (s, 3H), 2.91 (br, 1H), 3.81 (s, 3H), 4.58 (dd, *J* = 15.4, 5.7 Hz, 1H), 4.78 (dd, *J* = 15.4, 5.7 Hz, 1H), 5.94 (dd, *J* = 5.2, 1.1 Hz, 1H), 6.18 (dd, *J* = 16.0, 5.2 Hz, 1H), 6.60 (dd, *J* = 16.0, 1.1 Hz, 1H), 6.84 (d, *J* = 9.2 Hz, 2H), 7.11 (t, *J* = 5.7 Hz, 1H), 7.21–7.28 (m, 7H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.10, 44.98, 55.30, 70.64, 108.59, 113.99, 123.84, 127.21, 127.32, 127.91, 128.57, 128.75, 130.81, 138.47, 155.50, 159.54, 160.49, 170.44. Anal. Calcd for $C_{22}H_{22}ClN_3O_2S$: C, 61.75; H, 5.18; N, 9.82. Found: C, 61.37; H, 5.32; N, 9.88.

1-{6-Chloro-4-[(4-chlorophenylmethyl)amino]-2-(methylsulfanyl)}pyrimidin-5-yl}-3-(4-methoxyphenyl)prop-2-en-1-ol (3j): a white solid; mp 132–134 °C (hexane/CH_2Cl_2); IR (KBr) 3384, 1608 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.42 (s, 3H), 3.11 (d, *J* = 2.9 Hz, 1H), 3.82 (s, 3H), 4.52 (dd, *J* = 15.4, 5.2 Hz, 1H), 4.76 (dd, *J* = 15.4, 6.3 Hz, 1H), 5.93–5.95 (m, 1H), 6.15 (dd, *J* = 16.0, 5.1 Hz, 1H), 6.57 (dd, *J* = 16.0, 1.1 Hz, 1H), 6.86 (d, *J* = 9.2 Hz, 2H), 7.12 (dd, *J* = 6.3, 5.2 Hz, 1H), 7.17 (s, 4H), 7.26 (d, *J* = 9.2 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.10, 44.25, 55.31, 70.47, 108.71, 114.03, 123.73, 127.85, 128.62, 128.68 (two overlapped Cs), 130.70, 132.90, 137.02, 155.52, 159.56, 160.43, 170.43. Anal. Calcd for $C_{22}H_{21}Cl_2N_3O_2S$: C, 57.15; H, 4.58; N, 9.09. Found: C, 57.16; H, 4.63; N, 9.04.

1-[6-Chloro-4-(cyclopropylamino)-2-(methylsulfanyl)pyrimidin-5-yl]-3-(4-methoxyphenyl)prop-2-en-1-ol (3k): a colorless viscous oil; R_f 0.33 (AcOEt/hexane 1:5); IR (neat) 3339, 3209, 1608 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.45–0.51 (m, 2H), 0.77–0.80 (m, 2H), 2.53 (s, 3H), 2.84–2.87 (m, 1H), 3.15 (d, *J* =2.9 Hz, 1H), 3.80 (s, 3H), 5.87 (d, *J* = 5.7 Hz, 1H), 6.10 (dd, *J* = 16.0, 5.7 Hz, 1H), 6.56 (dd, *J* = 16.0, 1.1 Hz, 1H), 6.84 (d, *J* = 8.6 Hz, 2H), 6.90 (d, *J* = 2.9 Hz, 1H), 7.28 (d, *J* = 8.6 Hz, 2H); ^{13}C NMR

(125 MHz, $CDCl_3$) δ 7.00, 7.47, 14.09, 24.01, 55.27, 70.63, 108.67, 114.01, 123.78, 127.87, 128.82, 130.82, 155.21, 159.21, 161.85, 170.34. MR–MS (ESI). Calcd for $C_{18}H_{21}ClN_3O_2S$ (M+H): 378.1043. Found: *m*/*z* 378.1032.

Typical Procedure for the Preparation of 2-[(Pyrimidin-2-yl)amino]acetonitriles (5). 2-({5-Chloro-4-[1-hydroxy-3-(4-methoxyphenyl)prop-2-enyl]-2-(methylsulfanyl)pyrimidin-2-yl}-amino)acetonitrile (5d). A mixture of **2d** (0.36 g, 1.0 mmol) and 2-aminioacetonitrile hydrochloride (94 mg, 1.0 mmol) in DMF (6 mL) containing Et_3N (0.20 g, 2.0 mmol) was stirred for 150 h at rt. The mixture was worked up as described for the preparation of **3a** and the residue was purified by column chromatography on SiO_2 (Et_2O/hexane 3:2) to give **5d** (0.20 g, 53%); a white solid; mp 151–154 °C (hexane/CH_2Cl_2); IR (KBr) 3336, 2241, 1608 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.56 (s, 3H), 3.32 (br s, 1H), 3.80 (s, 3H), 4.27 (dd, *J* = 17.2, 5.2 Hz, 1H), 4.40 (dd, *J* = 17.2, 6.3 Hz, 1H), 5.89 (br s, 1H), 6.14 (dd, *J* = 16.0, 6.3 Hz, 1H), 6.60 (d, *J* = 16.0 Hz, 1H), 6.84 (d, *J* = 8.6 Hz, 2H), 7.24 (dd, *J* = 6.3, 5.2 Hz, 1H), 7.27 (d, *J* = 8.6 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.17, 29.42, 55.30, 70.78, 110.01, 114.04, 116.29, 123.15, 127.99, 128.46, 131.52, 156.17, 159.69, 159.89, 170.79. Anal. Calcd for $C_{17}H_{17}ClN_4O_2S$: C, 54.18; H, 4.55; N, 14.87. Found: C, 53.93; H, 4.61; N, 14.95.

2-({5-Chloro-4-[1-hydroxy-3-(4-methylphenyl)prop-2-enyl]-2-(methylsulfanyl)pyrimidin-2-yl}-amino)acetonitrile (5b): a pale-yellow solid; mp 163–165 °C (hexane/CH_2Cl_2); IR (KBr) 3332, 2242 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.33 (s, 3H), 2.56 (s, 3H), 3.45 (br s, 1H), 4.25 (dd, *J* = 17.2, 5.2 Hz, 1H), 4.39 (dd, *J* = 17.2, 6.9 Hz, 1H), 5.89 (d, *J* = 5.7 Hz, 1H), 6.22 (dd, *J* = 16.0, 5.7 Hz, 1H), 6.62 (d, *J* = 16.0 Hz, 1H), 7.12 (d, *J* = 8.0 Hz, 2H), 7.23–7.27 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.17, 21.20, 29.42, 70.60, 109.95, 116.27, 124.34, 126.61, 129.34, 131.77, 132.93, 138.23, 156.11, 159.89, 170.78. Anal. Calcd for $C_{17}H_{17}ClN_4OS$: C, 56.58; H, 4.75; N, 15.53. Found: C, 56.22; H, 4.81; N, 15.30.

Typical Procedure for the Preparation of 7,8-Dihydropyrido[2,3-*d*]pyrimidine Derivatives (4) and (6). 8-Butyl-4-chloro-2-(methylsulfanyl)-7-phenyl-7,8-dihydropyrido[2,3-*d*]pyrimidine (4a). To a stirred solution of **3a** (0.38 g, 1.1 mmol) in THF (4 mL) containing Et_3N (0.21 g, 2.1 mmol) at 0 °C was added MsCl (0.12 g, 1.1 mmol) dropwise. After stirring was continued for 1 h, saturated aqueous NH_4Cl (15 mL) was added and the mixture was extracted with AcOEt (3 × 10 mL). The combined extracts were washed with brine (10 mL), dried (Na_2SO_4), and concentrated by evaporation. The residue was purified by column chromatography on SiO_2 to give **4a** (0.22 g, 64%); a yellow oil; R_f 0.46 (AcOEt/hexane 1:10); IR (neat) 1645, 1566 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.87 (t, *J* = 7.6 Hz, 3H), 1.21–1.31 (m, 2H), 1.35–1.42 (m, 1H), 1.54–1.62 (m, 1H), 2.48 (s, 3H), 2.82–2.88 (m, 1H), 3.89–3.95 (m, 1H), 5.40 (d, *J* = 3.8 Hz, 1H), 5.58 (dd, *J* = 9.9, 4.6 Hz, 1H), 6.52 (d, *J* = 9.9 Hz, 1H), 7.28–7.42 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.81, 14.14, 20.67, 28.31, 45.85, 64.05, 105.07, 118.00, 125.17, 126.73, 128.47, 129.06,

141.84, 152.87, 158.30, 170.11. MR–MS (EI). Calcd for $C_{18}H_{20}ClN_3S$ (M): 345.1066. Found: *m/z* 345.1050. Anal. Calcd for $C_{18}H_{20}ClN_3S$: C, 62.51; H, 5.83; N, 12.15. Found: C, 62.49; H, 5.83; N, 12.03.

4-Chloro-2-(methylsulfanyl)-7-phenyl-8-(phenylmethyl)-7,8-dihydropyrido[2,3-*d*]pyrimidine (4b): a yellow solid; mp 153–155 °C (hexane/CH_2Cl_2); IR (KBr) 1649, 1564 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.45 (s, 3H), 3.62 (d, *J* = 15.3 Hz, 1H), 5.26 (d, *J* = 3.8 Hz, 1H), 5.55 (dd, *J* = 9.9, 3.8 Hz, 1H), 5.79 (d, *J* = 15.3 Hz, 1H), 6.55 (d, *J* = 9.9 Hz, 1H), 7.20–7.41 (m, 10H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.22, 47.38, 62.37, 105.06, 117.87, 125.36, 126.94, 127.62, 127.97, 128.59, 128.74, 129.16, 136.18, 141.05, 153.41, 158.61, 170.30. MR–MS (EI). Calcd for $C_{21}H_{18}ClN_3S$ (M): 379.0910. Found: *m/z* 379.0892. Anal. Calcd for $C_{21}H_{18}ClN_3S$: C, 66.39; H, 4.78; N, 11.06. Found: C, 66.25; H, 4.87; N, 10.94.

4-Chloro-8-(2-methoxyethyl)-2-(methylsulfanyl)-7-phenyl-7,8-dihydropyrido[2,3-*d*]pyrimidine (4c): a yellow oil; R_f 0.38 (AcOEt/hexane 2:15); IR (neat) 1645, 1566 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.47 (s, 3H), 3.06–3.13 (m, 1H), 3.31 (s, 3H), 3.35–3.39 (m, 1H), 3.63–3.68 (m, 1H), 4.04–4.08 (m, 1H), 5.57–5.59 (m, 2H), 6.51 (dd, *J* = 11.5, 3.1 Hz, 1H), 7.28 (d, *J* = 7.6 Hz, 2H), 7.32 (t, *J* = 7.6 Hz, 1H), 7.38 (t, *J* = 7.6 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.15, 45.47, 58.98, 65.22, 70.16, 105.44, 117.67, 125.70, 126.93, 128.46, 129.08, 141.75, 152.86, 158.34, 170.05. HR–MS (EI). Calcd for $C_{17}H_{18}ClN_3OS$ (M): 347.0859. Found: *m/z* 347.0857. Anal. Calcd for $C_{17}H_{18}ClN_3OS$: C, 58.70; H, 5.22; N, 12.08. Found: C, 58.65; H, 5.23; N, 12.09.

4-Chloro-8-methyl-7-(4-methylphenyl)-2-(methylsulfanyl)-7,8-dihydropyrido[2,3-*d*]pyrimidine (4d): a yellow oil; R_f 0.37 (AcOEt/hexane 1:15); IR (neat) 1645, 1567 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 2.35 (s, 3H), 2.49 (s, 3H), 2.91 (s, 3H), 5.26 (dd, *J* = 4.3, 1.4 Hz, 1H), 5.57 (dd, *J* = 10.1, 4.3 Hz, 1H), 6.53 (dd, *J* = 10.4, 1.4 Hz, 1H), 7.15 (d, *J* = 8.1 Hz, 2H), 7.18 (d, *J* = 8.1 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 14.18, 21.15, 33.90, 65.94, 105.22, 117.94, 125.42, 126.65, 129.78, 138.31, 138.45, 152.73, 158.52, 170.25. HR–MS (EI). Calcd for $C_{16}H_{16}ClN_3S$ (M): 317.0753. Found: *m/z* 317.0748. Anal. Calcd for $C_{16}H_{16}ClN_3S$: C, 60.46; H, 5.07; N, 13.22. Found: C, 60.26; H, 5.12; N, 13.01.

4-Chloro-8-[(3,4-dichlorophenyl)methyl]-7-(4-methylphenyl)-2-(methylsulfanyl)-7,8-dihydropyrido-[2,3-*d*]pyrimidine (4e): a pale-yellow amorphous powder; R_f 0.49 (AcOEt/hexane 1:15); IR (neat) 1646, 1566 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 2.36 (s, 3H), 2.44 (s, 3H), 3.75 (d, *J* = 15.5 Hz, 1H), 5.20 (dd, *J* = 4.3, 1.3 Hz, 1H), 5.51 (d, *J* = 15.5 Hz, 1H), 5.57 (dd, *J* = 10.0, 4.3 Hz, 1H), 6.56 (dd, *J* = 10.0, 1.3 Hz, 1H), 7.04 (dd, *J* = 8.2, 1.9 Hz, 1H), 7.11 (d, *J* = 8.0 Hz, 2H), 7.18 (d, *J* = 8.0 Hz, 2H), 7.24 (d, *J* = 1.9 Hz, 1H), 7.38 (d, *J* = 8.2 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.24, 21.17, 46.81, 62.80, 105.30, 117.82, 125.53, 126.92, 127.28, 129.83, 129.91, 130.65, 131.60, 132.75, 136.81, 137.83, 138.83, 153.56, 158.46, 170.39. HR-MS (ESI). Calcd for $C_{22}H_{19}Cl_3N_3S$ (M+H): 462.0365. Found: *m/z* 462.0350. Anal. Calcd for $C_{22}H_{18}Cl_3N_3S$: C, 57.09; H, 3.92; N, 9.08. Found: C, 56.76; H, 4.05; N, 9.33.

4-Chloro-7-(4-chlorophenyl)-8-methyl-2-(methylsulfanyl)-7,8-dihydropyrido[2,3-*d*]pyrimidine (4f): a pale-yellow solid; mp 96–99 °C (hexane/CH_2Cl_2); IR (KBr) 1645, 1568 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.50 (s, 3H), 2.91 (s, 3H), 5.30 (dd, *J* = 4.6, 1.7 Hz, 1H), 5.55 (dd, *J* = 9.7, 4.6 Hz, 1H), 6.56 (dd, *J* = 9.7, 1.7 Hz, 1H), 7.22 (d, *J* = 8.6 Hz, 2H), 7.36 (d, *J* = 8.6 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.17, 33.93, 65.55, 104.97, 118.45, 124.59, 128.03, 129.32, 134.40, 139.60, 152.99, 158.40, 170.49. HR–MS (EI). Calcd for $C_{15}H_{13}Cl_2N_3S$ (M): 337.0207. Found: *m*/*z* 337.0195. Anal. Calcd for $C_{15}H_{13}Cl_2N_3S$: C, 53.26; H, 3.87; N, 12.42. Found: C, 53.17; H, 3.96; N, 12.34.

4-Chloro-7-(4-chlorophenyl)-2-(methylsulfanyl)-8-(2-phenylethyl)-7,8-dihydropyrido[2,3-*d*]pyrimidine (4g): a pale-yellow solid; mp 100–104 °C (hexane/CH_2Cl_2); IR (KBr) 1650, 1568 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.53 (s, 3H), 2.59–2.65 (m, 1H), 2.93–2.96 (m, 1H), 3.09–3.12 (m, 1H), 3.99–4.02 (m, 1H), 5.10 (dd, *J* = 4.6, 1.7 Hz, 1H), 5.45 (dd, *J* = 10.3, 4.6 Hz, 1H), 6.53 (dd, *J* = 10.3, 1.7 Hz, 1H), 7.11–7.36 (m, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.25, 32.95, 48.39, 64.30, 105.02, 118.27, 124.65, 126.55, 128.28, 128.61, 128.72, 129.32, 134.47, 138.78, 140.23, 153.13, 158.08, 170.50. HR–MS (ESI). Calcd for $C_{22}H_{20}Cl_2N_3S$ (M+H): 428.0755. Found: *m*/*z* 428.0752. Anal. Calcd for $C_{22}H_{19}Cl_2N_3S$: C, 61.68; H, 4.47; N, 9.81. Found: C, 61.40; H, 4.72; N, 9.70.

4-Chloro-7-(4-methoxyphenyl)-8-methyl-2-(methylsulfanyl)-7,8-dihydropyrido[2,3-*d*]pyrimidine (4h): a yellow oil; R_f 0.63 (AcOEt/hexane 1:2); IR (neat) 1645, 1608, 1567 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.49 (s, 3H), 2.90 (s, 3H), 3.81 (s, 3H), 5.25 (d, *J* = 4.0 Hz, 1H), 5.57 (dd, *J* = 9.7, 4.0 Hz, 1H), 6.55 (d, *J* = 9.7 Hz, 1H), 6.89 (d, *J* = 8.6 Hz, 2H), 7.19 (d, *J* = 8.6 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.14, 33.76, 55.32, 65.52, 105.14, 114.36, 117.84, 125.38, 128.01, 133.42, 152.69, 158.34, 159.75, 170.20. HR–MS (EI). Calcd for $C_{16}H_{16}ClN_3OS$ (M): 333.0703. Found: *m*/*z* 333.0693. Anal. Calcd for $C_{16}H_{16}ClN_3OS$: C, 61.68; H, 4.47; N, 9.81. Found: C, 57.32; H, 5.02; N, 12.51.

4-Chloro-7-(4-methoxyphenyl)-2-(methylsulfanyl)-8-(phenylmethyl)-7,8-dihydropyrido[2,3-*d*]pyrimidine (4i): a yellow oil; R_f 0.50 (AcOEt/hexane 2:15); IR (neat) 1645, 1608, 1563 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.44 (s, 3H), 3.64 (d, *J* = 14.9 Hz, 1H), 3.82 (s, 3H), 5.20 (d, *J* = 4.6 Hz, 1H), 5.53 (dd, *J* = 9.7, 4.6 Hz, 1H), 5.76 (d, *J* = 14.9 Hz, 1H), 6.55 (d, *J* = 9.7 Hz, 1H), 6.90 (d, *J* = 8.6 Hz, 2H), 7.17 (d, *J* = 8.6 Hz, 2H), 7.21 (d, *J* = 7.4 Hz, 2H), 7.29 (t, *J* = 7.4 Hz, 1H), 7.34 (t, *J* = 7.4 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.21, 47.20, 55.34, 61.70, 105.06, 114.41, 117.64, 125.57, 127.58, 127.96, 128.32, 128.71, 133.30, 136.23, 153.33, 158.47, 159.80, 170.23. HR–MS (EI). Calcd for $C_{22}H_{20}ClN_3OS$ (M): 409.1016. Found: *m*/*z* 409.1014. Anal. Calcd for $C_{22}H_{20}ClN_3OS$: C, 64.46; H, 4.92; N, 10.25. Found: C, 64.39; H, 5.01; N, 10.28.

4-Chloro-8-(4-chlorophenylmetyl)-7-(4-methoxyphenyl)-2-(methylsulfanyl)-7,8-dihydropyrido[2,3-*d*]pyrimidine (4j): a white solid; mp 101–104 °C (hexane/CH_2Cl_2); IR (KBr) 1649, 1610, 1567 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.43 (s, 3H), 3.67 (d, *J* = 15.5 Hz, 1H), 3.82 (s, 3H), 5.17 (d, *J* = 4.0 Hz, 1H),

5.54 (dd, *J* = 9.7, 4.0 Hz, 1H), 5.64 (d, *J* = 15.5 Hz, 1H), 6.55 (d, *J* = 9.7 Hz, 1H), 6.89 (d, *J* = 8.6 Hz, 2H), 7.14 (d, *J* = 8.0 Hz, 2H), 7.15 (d, *J* = 8.0 Hz, 2H), 7.29 (d, *J* = 8.6 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.22, 46.72, 55.36, 61.91, 105.11, 114.45, 117.65, 125.55, 128.28, 128.86, 129.31, 130.06, 133.35, 134.79, 153.41, 158.37, 159.85, 170.26. Anal. Calcd for $C_{22}H_{19}Cl_2N_3OS$: C, 59.46; H, 4.31; N, 9.46. Found: C, 59.30; H, 4.37; N, 9.32.

4-Chloro-8-cyclopropyl-7-(4-methoxyphenyl)-2-(methylsulfanyl)-7,8-dihydropyrido[2,3-*d*]pyrimidine (4k): a yellow oil; R_f 0.45 (AcOEt/hexane 1:6); IR (neat) 1641, 1608, 1563 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.64–0.67 (m, 1H), 0.71–0.74 (m, 1H), 0.77–0.81 (m, 1H), 2.27–2.30 (m, 1H), 1.03–1.06 (m, 1H), 2.50 (s, 3H), 3.79 (s, 3H), 5.22 (d, *J* = 4.6 Hz, 1H), 5.70 (dd, *J* = 9.7, 5.2 Hz, 1H), 5.61 (d, *J* = 9.7 Hz, 1H), 6.87 (d, *J* = 8.6 Hz, 2H), 7.21 (d, *J* = 8.6 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 6.46, 11.15, 14.17, 28.83, 55.30, 62.85, 106.63, 114.25, 118.14, 126.16, 128.10, 132.70, 152.95, 159.75 (two overlapped Cs), 170.03. HR–MS (EI). Calcd for $C_{18}H_{18}ClN_3OS$ (M): 359.0859. Found: *m/z* 359.0842. Anal. Calcd for $C_{18}H_{18}ClN_3OS$: C, 60.08; H, 5.04; N, 11.68. Found: C, 60.12; H, 5.34; N, 11.67.

[4-Chloro-7-(4-methylphenyl)-2-(methylsulfanyl)-7,8-dihydropyrido[2,3-*d*]pyrimidin-8-yl]acetonitrile (6b): a white solid; mp 172–175 °C (hexane/CH_2Cl_2); IR (KBr) 2248, 1637, 1564 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.37 (s, 3H), 2.52 (s, 3H), 3.75 (d, *J* = 17.8 Hz, 1H), 4.86 (d, *J* = 17.8 Hz, 1H), 5.50 (dd, *J* = 4.0, 1.7 Hz, 1H), 5.65 (dd, *J* = 10.3, 4.0 Hz, 1H), 6.59 (dd, *J* = 10.3, 1.7 Hz, 1H), 7.23 (s, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.24, 21.18, 33.29, 63.99, 105.76, 114.72, 117.67, 125.47, 127.17, 130.15, 136.25, 139.50, 153.75, 157.30, 170.70. HR–MS (EI). Calcd for $C_{17}H_{15}ClN_4S$ (M): 342.0706. Found: *m/z* 342.0706. Anal. Calcd for $C_{17}H_{15}ClN_4S$: C, 59.56; H, 4.41; N, 16.34. Found: C, 59.59; H, 4.48; N, 16.18.

[4-Chloro-7-(4-methoxyphenyl)-2-(methylsulfanyl)-7,8-dihydropyrido[2,3-*d*]pyrimidin-8-yl]acetonitrile (6d): a pale-yellow solid; mp 156–158 °C (hexane/CH_2Cl_2); IR (KBr) 2245, 1641, 1612, 1562 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.52 (s, 3H), 3.77 (d, *J* = 17.2 Hz, 1H), 4.86 (d, *J* = 17.2 Hz, 1H), 3.82 (s, 3H), 5.48 (d, *J* = 1.7 Hz, 1H), 5.65 (dd, *J* = 10.3, 4.0 Hz, 1H), 6.59 (dd, *J* = 10.3, 1.7 Hz, 1H), 6.93 (d, *J* = 8.6 Hz, 2H), 7.27 (d, *J* = 8.6 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.25, 33.21, 55.37, 63.63, 105.73, 114.73, 114.76, 117.63, 125.52, 128.63, 131.27, 153.75, 157.21, 160.40, 170.70. HR–MS (EI). Calcd for $C_{17}H_{15}ClN_4OS$ (M): 358.0655. Found: *m/z* 358.0651. Anal. Calcd for $C_{17}H_{15}ClN_4OS$: C, 56.90; H, 4.21; N, 15.61. Found: C, 56.80; H, 4.18; N, 15.49.

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