

4-Aminopyrimidine-5-carbaldehydes as intermediates in a Friedländer type synthesis of 7-arylpyrido[2,3-*d*]pyrimidines

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Abstract

A study of formylation of 6-aminopyrimidines leads to the conclusion that the formylation at C5 occurs only when there is no contribution of heteroaromaticity in the pyrimidine ring and that the corresponding pyrimidoformamides are formed in heteroaromatic pyrimidines. Once 4-aminopyrimidin-4(3*H*)-one-5-carboxaldehydes were prepared, a series of 7-arylpyrido[2,3-*d*]pyrimidines derivatives were synthesized by a Friedländer type reaction with acetophenones under solvent-free conditions and in the presence of BF₃-Et₂O. The yields of 7-arylpyrido[2,3-*d*]pyrimidines range from moderate to good and the reaction times were quite short.

Keywords: Nitrogenated heterocycles, acylation, cyclocondensation, solvent free, regioselectivity

Introduction

Nitrogen heterocycles have received a great deal of attention in the literature as a result of their role as pharmacophores of great historical significance. Among these heterocyclic systems, especially those containing pyridine have been the subject of expanding research efforts in heteroaromatic and biological chemistry.¹ The pyrido[2,3-*d*]pyrimidine heterocycles (a.k.a. 5-deazapteridines), which are those annelated to a pyrimidine ring, are of paramount importance because of their wide range of biological^{1a,2} and pharmaceutical applications (i.e., bronchodilators, vasodilators) and their anti-allergic, cardiogenic, antihypertensive, and hepatoprotective activities.³ Some of them have shown properties as antitumour, antibacterial, analgesic or CNS depressants.⁴

The synthesis of pyrido[2,3-*d*]pyrimidines has been typically performed by annelation of the pyrimidine ring on the pyridine or vice versa,⁵ and these methods include diverse procedures based on the Michael addition-cyclodehydration strategy,^{1,5f} the three-component one-pot synthesis,^{2,6} the route *via* the aza-Wittig reaction⁷ from iodouracils, having a formamidine or acetamidine moiety with various acetylene derivatives.⁸ Aside from the traditional methodologies, more recent methods include a microwave-assisted one-pot synthesis^{3,4c} and a procedure that involves ultrasound irradiation without a catalyst.⁹ Although, the synthesis of this bicyclic system is well documented, most of the synthetic methods rely on cyclocondensation that usually require drastic conditions, long reaction times and complex synthetic pathways. Thus, the search for new, fast routes of synthesis of this kind of molecules remains of considerable importance.

In the course of our synthetic studies of simple nitrogen-containing heterocycles, we have already reported the synthesis of functionalized pyrido[2,3-*d*]pyrimidines *via* a selective cyclocondensation reaction between 6-aminopyrimidines and Mannich bases (β -dimethylaminopropiophenone hydrochlorides), 3-formylchromone, 2-dimethylaminomethylentetralone hydrochloride, chalcones and methylene-active compounds,¹⁰ and also by using microwave-assisted multicomponent synthesis.¹¹

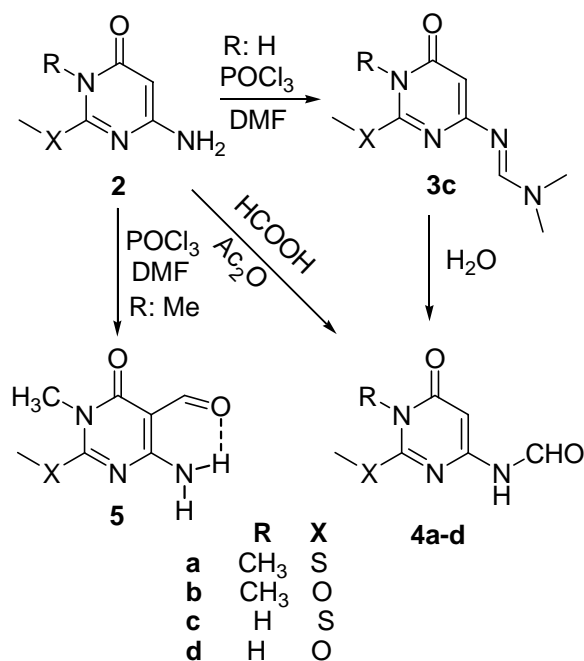
On the other hand, the Friedländer reaction is a well-known method for the preparation of heteroannulated compounds,¹² and we consider that it is one of the most useful methods for the preparation of pyridopyrimidines and related bicyclic systems. This consists of the reaction between an aromatic or heteroaromatic ortho-amino-carbaldehyde and an aldehyde or ketone bearing an α -methylene moiety. In most cases, this cyclocondensation reaction type was carried out under conventional methods and with longer reaction times. In this way, the possibility of performing reactions under solvent-free conditions is particularly attractive because of its simplicity, lower environmental impact, and minimum reaction time, which can provide a rapid access to large libraries of diverse molecules.

Here we provide a simple and solvent-free method for the preparation of 7-arylpyrido[2,3-*d*]pyrimidines from 6-aminopyrimidines. We have previously prepared the corresponding 6-aminopyrimidin-5-carboxaldehydes in order to act as intermediates in a Friedländer reaction type.¹³

Results and Discussion

We have tried the preparation of 4-aminopyrimidin-5-carboxaldehydes from 6-aminopyrimidin-4(3*H*)-ones **2a-d**. Two classical formylation reagents, the acetic anhydride/formic acid mixture¹⁴ or the Vilsmeier reagent,¹⁵ have been used (see Scheme 1). The reaction of the 6-aminopyrimidines with an acetic anhydride/formic acid mixture led in all cases to the corresponding 6-formamidepyrimidine derivatives **4** in good to excellent yields.

On the other hand, the use of Vilsmeier's reagent rendered different results depending on the starting material, reaction conditions and work-up (Scheme 1). Thus, the formylation at C-5 in the pyrimidine nucleus was effective only when the 3-methyl derivatives **2a,b** were used. In the case of the *3H* analogues **2c,d**, the different attempts of formylation at C5 with Vilsmeier's reagent resulted in all cases in attack at the 6-amino group. Depending on the work-up conditions, one may i) recover the starting material **2c,d**, ii) isolate the corresponding amidoderivatives **4c,d** or iii) produce the (*N,N*-dimethyl)amidine derivative **3c** (on work-up with ethanol at room temperature for 48 h).



Scheme 1. Formylation reactions of 6-aminopyrimidin-4(*3H*)-ones **2**.

This marked difference in the behaviour of the N(3)-CH₃ vs. N(3)-H pyrimidines, **2a,b** vs. **2c,d**, respectively, is due to the nucleophilic characters of C5 and the 6-amino group. For **2a,b** that amino group is part of an amide vinylogous moiety and C5 is the most nucleophilic site, while for **2c,d**, the possibility of lactam-lactim tautomerism gives this compound some heteroaromatic character and results in a higher nucleophilic character of the amino group. In fact, the use of Vilsmeier conditions to the heteroaromatic 6-chloro-2-(methylthio)pyrimidin-4-amine, **2e**, or 4,6-dimethoxypyrimidin-2-amine, **2f**, affords reaction at the amino group and yields **3e** and **4f**, respectively (Figure 1).

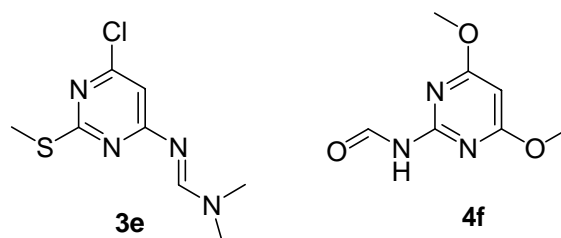
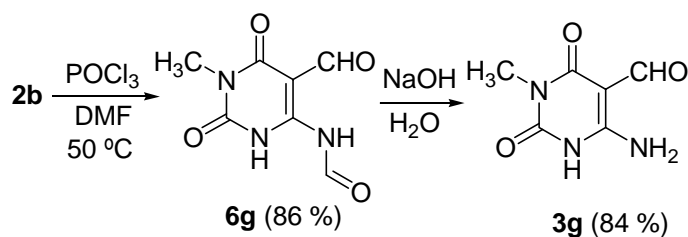


Figure 1. Compounds isolated by Vilsmeier formylation of 6-amino-4-chloro-2-methylthiopyrimidine **2e** and 2-amino-4,6-dimethoxypyrimidine **2f**.

Optimized conditions for the preparation of the 5-formylpyrimidine **5a** (Scheme 2) involved warming to 50 °C for 18 h, quenching with ice and neutralizing with NaOH, and a second heating for 1 h, and this protocol resulted in a 88% yield. The application of this protocol to the preparation of the 6-amino-1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-carbaldehyde **1** resulted in a 98 % yield; an improvement over the previously reported 90% yield.¹⁶ For the 2-methoxypyrimidine **2b**, the reaction proceeded under such conditions with hydrolysis of the methoxy group and formylation at both C5 and 6-NH₂ giving **6g** (86% yield), which can be hydrolyzed in aqueous NaOH to afford the known 6-amino-3-methyl-2,4-dioxo-1,2,3,4-tetrahydro-5-pyrimidine-carbaldehyde¹⁷ **3g** in 84% yield (Scheme 2). Thus, in order to prepare the 5-formyl derivative **5b** from **2b**, the reaction with the Vilsmeier reagent was carried out at 0 °C to afford **5b** in 70% yield.

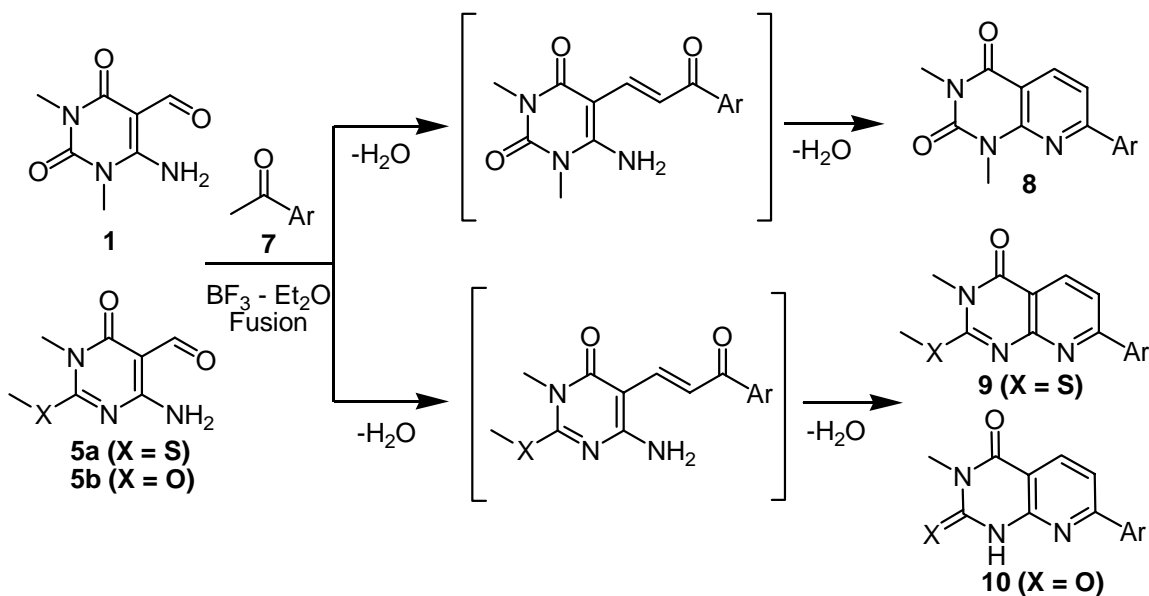


Scheme 2. Formylation of 6-amino-2-methoxy-3-methylpyrimidin-4(3*H*)-one **2b** under the optimized conditions used in the preparation of compound **5a** from **2a**.

The ¹H NMR spectra of **1**, **5a,b** and **3g** show two broad singlets for the protons of the 4-NH₂ group due to the intramolecular hydrogen bond between the H and the oxygen atom of the 5-CHO group (Experimental and Scheme 1). 4-Aminopyrimidine-5-carbaldehydes **1**, **5a,b** were reacted with acetophenones **7** under different conditions. The use of an equimolar ratio and catalytic amount of BF₃-Et₂O (3 drops) through a solvent-free fusion method was appropriate to render the desired 7-arylpyrido[2,3-*d*]pyrimidines **8** - **10** in moderate to good yields within a few seconds. The pyridopyrimidines were filtrated and purified by recrystallization or by column chromatography.

To the best of our knowledge, $\text{BF}_3\text{-Et}_2\text{O}$ has been used in the syntheses of several chalcones through a Claisen-Schmidt reaction.¹⁸ Here the 7-arylpyrido[2,3-*d*]pyrimidines were obtained through the initial formation of the corresponding chalcones by an acid-catalyzed Claisen-Schmidt reaction and subsequent intramolecular cyclocondensation between amino and carbonyl groups to give 7-arylpyrido[2,3-*d*]pyrimidines **8** - **10** (Scheme 3). It is important to note that $\text{BF}_3\text{-Et}_2\text{O}$ can be used in the presence of ester and amide functional groups. The use of basic catalytic conditions resulted in hydrolysis. On the contrary, the thermal cyclization of compounds **5b** occurs through the hydrolysis of the 2-methoxy group to form **10**.

Something similar happened in other previous acid reactions in presence of a nucleophile as water formed in the condensation step.¹⁹ Compounds **10**, which are difficult to produce from the corresponding 6-amino-3-methyluracil, can also be obtained from the 6-amino-3-methyl-2,4-dioxo-1,2,3,4-tetrahydro-5-pyrimidinecarbaldehyde **3g**.



Scheme 3. Solvent-free reaction of 6-aminopyrimidine-5-carbaldehydes and acetophenones to 7-arylpyrido[2,3-*d*]pyrimidines.

Table 1. Solvent-free preparation of 7-arylpyrido[2,3-*d*]pyrimidines: Melting points (°C) and yields

Entry	Ar	Compound 8 from 1		Compound 9 from 5a		Compound 10 from 5b	
		M.p. ^a	%	M.p.	%	M.p.	%
a	C ₆ H ₅	157-159 (156-157)	65	129-131	75	291-293	70
b	4-H ₃ CC ₆ H ₄	175-177 (173-174)	50	189-191	70	>300	60
c	4-H ₃ COC ₆ H ₄	163-165 (164)	65	196-198	70	>300	70
d	3,4,5- (H ₃ CO) ₃ C ₆ H ₂	211-213	40	211-213	70	297-299	60
e	4-C ₆ H ₅ C ₆ H ₄	233-235	60	222-224	50	>300	40
f	4-HOC ₆ H ₄	>300 dec.	40	249-251	80	>300	60
g	4-O ₂ NC ₆ H ₄	283-285	50	272-274	70	--	--
h	4-ClC ₆ H ₄	138-140 (139-140)	40	219-221	70	313-315	60
i	4-BrC ₆ H ₄	217-219	40	206-208	80	310-312	50
j	4-FC ₆ H ₄	207-209	60	202-204	70	295-297	60
k	Coumaryl	284-286	60	217-219	70	--	--

^a M.p. reported by Troschuz et al.^{5f} are given in parentheses.

The structures of compounds **8**, **9** and **10** were confirmed by spectroscopic analysis. All products show NMR spectra that are in agreement with the proposed structures. The assignment of carbon atoms was based on DEPT-135 measurements along with 2-dimensional HMBC and HSQC (¹H-¹³C) experiments. All sets of compounds **8** and **9** present similar spectroscopic profiles. For example, in the ¹H NMR spectrum of compound **8a** the signals of H-6 and H-5 in the pyridine ring appear at 7.66 and 8.49 ppm respectively as two doublets with $J_{ortho} = 8.03$ Hz, and in addition to the heteronuclear correlation observed in the HMBC experiment between signal assigned to C(4) with those to N(3)-CH₃ and H-5.

Regarding compounds **10** the spectroscopic data confirm the hydrolysis of the methoxy group at C(2), the corresponding signal for the H-1 proton of the pyrimidine ring. Finally, the structure of the 7-arylpyrido[2,3-*d*]pyrimidines was unambiguously confirmed by X-ray diffraction analysis of compounds **8b**, **8e**, **10c** and **10j**.²⁰

Conclusions

We have shown that formylation of 6-aminopyrimidines can occur at the amino group in heteroaromatic pyrimidine systems, and it can occur at C5 if the heteroaromaticity of the pyrimidine ring is low. Using these 5-formylpyrimidine derivatives we have developed a new, rapid and simple methodology for the synthesis of several functionalized pyrido[2,3-

d]pyrimidines of potential biological importance in moderate to good yields. This method can be very useful for high-throughput synthesis. A particularly valuable feature of this method consists in the fact that, for the first time, the reaction was catalysed by BF₃-Et₂O. The advantages of our method compared to existing methods are short reaction times, solvent-free conditions, low cost and high tolerance of sensitive functional groups such as esters or amides.

Experimental Section

General. Melting points were determined in a Buchi Melting Point Apparatus and are reported uncorrected. The ¹H- and ¹³C NMR spectra were measured on Bruker Avance 400 spectrometers operating at 400 and 100 MHz, respectively, and using DMSO-*d*₆ as solvent and tetramethylsilane as internal standard. The mass-spectra were scanned on a Hewlett Packard HP Engine-5989 spectrometer (equipped with a direct inlet probe) which was operating at 70 eV. High Resolution Mass Spectra (HRMS) were recorded in a Waters Micromass AutoSpec NT spectrometer (STIUJA). The elemental analyses have been obtained using a LECO CHNS-900 and Thermo Finnigan FlashEA1112 CHNS-O (STIUJA) elemental analyzers.

General procedure A for the synthesis of *N*-pyrimidin-4-yl formamides with acetic anhydride/formic acid mixture

0.5 ml acetic anhydride, 0.15 ml formic acid and 1 mmol of the corresponding 6-aminopyrimidine were warmed for the specific time and temperature for each starting aminopyrimidine. The reaction was monitored by TLC (eluent CH₂Cl₂-MeOH, 9:1). After reaction of all the aminopyrimidine substrate, the mixture was dried under reduce pressure and the crude product was recrystallized from EtOH. The solid was filtered and washed with cool EtOH.

General procedure B for Vilsmeier formylation of 6-Aminopyrimidines

0.15 ml POCl₃ in 0.5 ml DMF was stirred in an ice bath for 15 minutes. Then, another 1.5 ml DMF and 1 mmol of the corresponding 6-aminopyrimidine were added to the cool solution. The reaction takes place at the corresponding temperature and time for each case. The reaction was monitored by TLC (eluent CH₂Cl₂-MeOH, 9:1). After complete consumption of the aminopyrimidine substrate, the mixture was poured into crushed ice and the solution was allowed to warm to room temperature and then brought to a boil and neutralized with NaOH. The heating continues for an hour and let it cooled to room temperature. The resulting precipitated was filtered, washed with water and recrystallized from EtOH.

6-Amino-1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-carbaldehyde 1. 0.155 g of 6-amino-1,3-dimethylpyrimidine-2,4(1*H*,3*H*)-dione reacts according to the general procedure B for 30 minutes at 50 °C. Yield of 98%, mp 195-198 °C, bibliographic mp 196-198 °C.¹⁶

***N,N*-Dimethyl-*N'*-[2-(methylthio)-6-oxo-1,6-dihydropyrimidin-4-yl]imidiformamide 3c.** 0.157 g of 6-amino-2-(methylthio)pyrimidin-4(3*H*)-one reacts according to the general procedure B at 0°C for 7 hour. White solid. Yield 60%, mp 161–162 °C. ¹H NMR (400 MHz, DMSO-*d*₆): δ = 2.56 (s, 3H, SCH₃); 3.41 (s, 3H, NCH₃); 3.43 (s, 3H, NCH₃); 6.38 (s, 1H, C₅-H); 8.92 (s, 1H, CH); 12.48 (s, 1H, NH). ¹³C NMR (100 MHz, DMSO-*d*₆): δ = 13.15 (SCH₃); 39.07 (NCH₃); 44.54 (NCH₃); 92.81 (C₅H); 152.05 (CH); 154.73 (C₆); 164.26 (C₄); 164.94 (C₂). IR (KBr) cm⁻¹ 3004 (NH *st*), 1646 (C=O *st*) 1594 (NH *δ*). MS (70 eV) *m/z* (%) 212 (M⁺, 42), 197 (28), 156 (12), 68 (25), 42 (100). HR-MS calc. for C₈H₁₂N₄OS 212.0725 found 212.0732.

***N'*-[6-Chloro-2-(methylthio)pyrimidin-4-yl]-*N,N*-dimethylimidiformamide 3e.** 0.175 g of 6-chloro-2-(methylthio)pyrimidin-4-amine, **2e**, reacts according to the general procedure B with the Vilsmeier's reagent for 1 hour and 30 minutes at 50°C. White solid, yield 61%, mp 98–99 °C. ¹H NMR (400 MHz, DMSO-*d*₆): δ = 2.46 (s, 3H, SCH₃); 3.02 (s, 3H, NCH₃); 3.15 (s, 3H, NCH₃); 6.52 (s, 1H, C₅-H); 8.66 (s, 1H, CH). ¹³C NMR (100 MHz, DMSO-*d*₆): δ = 13.56 (SCH₃); 34.76 (NCH₃); 40.84 (NCH₃); 107.92 (C₅); 157.70 (CH); 158.91 (C₆); 168.36 (C₄); 170.82 (C₂). MS (70 eV) *m/z* (%) 230 (M⁺, 100), 215 (18), 184 (18), 149 (31). HR-MS calc. for C₈H₁₁ClN₄S 230.0390 found 230.0393. Anal. Calcd for C₈H₁₁ClN₄S: C, 41.65; H, 4.99; N, 24.28; S, 13.90. Found: C, 42.14; H, 4.99; N, 24.30; S, 14.11.

***N*-[1-Methyl-2-(methylthio)-6-oxo-1,6-dihydropyrimidin-4-yl]formamide 4a.** 0.174 g of 6-amino-3-methyl-2-(methylthio)pyrimidin-4(3*H*)-one reacts according to the general procedure A at 50 °C for 10 minutes. White solid. Yield 75%, mp 255–258 °C. ¹H NMR (400 MHz, DMSO-*d*₆, 350 K): δ = 2.56 (s, 3H, CH₃-S); 3.33 (s, 3H, N₃-CH₃); 5.91 (s, 1H, C₅-H); 8.95 (s, 1H, CHO); 10.28 (s, 1H, C₄-NH). ¹³C NMR (100 MHz, DMSO-*d*₆, 350 K): δ = 14.13 (S-CH₃); 29.23 (N-CH₃); 89.57 (C₅); 163.22 (C₂); 153.42 (C₆); 161.19 (C₄); 161.30 (CHO). IR (KBr) cm⁻¹ 3004 (NH *st*), 1646 (C=O *st*) 1594 (NH *δ*). MS (70 eV) *m/z* (%) 199 (M⁺, 39); 171 (64); 68 (64); 57 (100). HR-MS calc. for C₇H₉N₃O₂S 199.0415 found 199.0420. Anal. Calcd for C₇H₉N₃O₂S: C, 42.25; H, 4.52; N, 21.10; S, 16.08. Found: C, 41.94; H, 4.52; N, 20.77; S, 15.76.

***N*-[2-Methoxy-1-methyl-6-oxo-1,6-dihydropyrimidin-4-yl]formamide 4b.** 0.155 g of 6-amino-2-methoxy-3-methylpyrimidin-4(3*H*)-one reacts according to the general procedure A at 50 °C for 15 minutes. White solid. Yield 90%, mp 214–215 °C. ¹H NMR (400 MHz, DMSO-*d*₆, 350 K): δ = 3.24 (s, 3H, N₃-CH₃); 4.00 (s, 3H, CH₃-O); 5.82 (s, 1H, C₅-H); 8.94 (s, 1H, CHO); 10.24 (s, 1H, C₄-NH). ¹³C NMR (100 MHz, DMSO-*d*₆, 350 K): δ = 26.62 (N-CH₃); 55.46 (O-CH₃); 90.32 (C₅); 156.91 (C₂); 154.98 (C₆); 158.54 (C₄); 162.45 (CHO). IR (KBr) cm⁻¹ 3377 (NH *st*), 1616 (C=O *st*) 1512 (NH *δ*). MS (70 eV) *m/z* (%) 183 (M⁺, 7); 155 (27); 125 (6); 40 (100). HR-MS calc. for C₇H₉N₃O₃ 183.0644 found 183.0645. Anal. Calcd for C₇H₉N₃O₃: C, 45.94; H, 4.92; N, 22.95. Found: C, 45.65; H, 5.15; N, 23.03.

***N*-[2-(Methylthio)-6-oxo-1,6-dihydropyrimidin-4-yl]formamide 4c.** 0.157 g of 6-amino-2-(methylthio)pyrimidin-4(3*H*)-one reacts according to the general procedure A at 50°C for 30 minutes. White solid. Yield 69%, mp 290-291 °C. ¹H NMR (400 MHz, DMSO-*d*₆, 350 K): δ = 2.50 (s, 3H, CH₃-S); 5.94 (s, 1H, C₅-H); 8.95 (s, 1H, CHO); 10.59 (s, 1H, C₄-NH); 12.44 (s, 1H, N₁-H). ¹³C NMR (100 MHz, DMSO-*d*₆, 350 K): δ = 12.49 (S-CH₃); 89.87 (C₅); 169.60 (C₂);

156.03 (C₆); 164.40 (C₄); 161.33 (CHO). IR (KBr) cm⁻¹ 3217 (NH *st*), 1645, 1684 (C=O *st*) 1515 (NH δ). MS (70 eV) *m/z* (%) 185 (M⁺, 60); 157 (86); 110 (25); 74 (29); 68 (100). HR-MS calc. for C₆H₇N₃O₂S 185.0259 found 185.0257. Anal. Calcd for C₆H₇N₃O₂S: C, 38.95; H, 3.78; N, 22.70; S, 17.30. Found: C, 39.32; H, 3.96; N, 22.35; S, 16.61.

***N*-(2-Methoxy-6-oxo-1,6-dihydropyrimidin-4-yl)formamide 4d.** 0.141 g of 6-amino-2-methoxypyrimidin-4(3*H*)-one reacts according to the general procedure A at reflux for 2 hours. White solid. Yield 74%, mp 226–228 °C. ¹H NMR (400 MHz, DMSO-*d*₆, 350 K): δ = 3.89 (s, 3H, CH₃-O); 5.77 (s, 1H, C₅-H); 8.92 (s, 1H, CHO); 10.52 (s, 1H, C₄-NH); 12.04 (s, 1H, N₁-H). ¹³C NMR (100 MHz, DMSO-*d*₆, 350 K): δ = 54.02 (O-CH₃); 88.27 (C₅); 164.38 (C₂); 156.40 (C₆); 158.56 (C₄); 161.31 (CHO). IR (KBr) cm⁻¹ 3007 (NH *st*), 1616 (C=O *st*) 1447 (NH δ). MS (70 eV) *m/z* (%) 169 (M⁺, 25); 141 (100); 111 (21); 68 (61). HR-MS calc. for C₆H₇N₃O₃ 169.0487 found 169.0482. Anal. Calcd for C₆H₇N₃O₃: C, 67.40; H, 4.90; N, 15.72. Found: C, 67.70; H, 4.86; N, 15.26.

***N*-(4,6-Dimethoxypyrimidin-2-yl)formamide 4f.** 0.155 g of 4,6-dimethoxypyrimidin-2-amine, **2f**, reacts according to the general procedure B with the Vilsmeier's reagent at different temperatures and time reactions. For 0 °C and 17 hours of reaction, yield: 76%. For 50 °C and 1 hour, yield: 72%. White solid, mp 124–126 °C. ¹H NMR (400 MHz, DMSO-*d*₆): δ = 3.95 (s, 6H, OCH₃); 5.90 (s, 1H, C₅-H); 9.35 (d, 8.5 Hz, 1H, CHO); 10.78 (d, 8.5 Hz, 1H, NH). ¹³C NMR (100 MHz, DMSO-*d*₆): δ = 54.10 (OCH₃); 84.11 (C₅); 156.83 (C₂); 163.50 (CHO); 171.58 (C₄ and C₆). IR (KBr) cm⁻¹: 3134 (NH *st*), 1697 (C=O *st*) 1401 (NH δ). MS (70 eV) *m/z* (%) 183 (M⁺, 22), 154 (100), 125 (25), 68 (29). HR-MS calc. for C₇H₉N₃O₃ 183.0642 found 183.0644.

4-Amino-1-methyl-2-(methylthio)-6-oxo-1,6-dihydropyrimidine-5-carbaldehyde 5a. 0.174 g of 6-Amino-3-methyl-2-(methylthio)pyrimidin-4(3*H*)-one reacts according to the general procedure B for 18 hours at 50 °C. White solid. Yield 88%, mp 226-228 °C. ¹H NMR (400 MHz, DMSO-*d*₆): δ = 2.55 (s, 3H CH₃-S); 3.31 (s, 3H, CH₃-N); 8.24 (s, 1H, NH₂); 8.91 (s, 1H, NH₂); 9.90 (s, 1H, CHO). ¹³C NMR (100 MHz, DMSO-*d*₆): δ = 14.48 (S-CH₃); 28.98 (N-CH₃); 94.33 (C₅); 167.78 (C₂); 160.06 (C₆); 162.06 (C₄); 188.52 (CHO). IR (KBr) cm⁻¹ 3375, 3272 (NH₂ *st*), 1630, 1605 (C=O *st*). MS (70 eV) *m/z* (%) 199 (M⁺, 24), 171 (100), 68 (62), 57 (64). HR-MS calc. for C₇H₉N₃O₂S 199.0415 found 199.0427.

4-Amino-2-methoxy-1-methyl-6-oxo-1,6-dihydropyrimidine-5-carbaldehyde 5b. 0.155 g of 6-Amino-2-methoxy-3-methylpyrimidin-4(3*H*)-one reacts according to the general procedure B for 4 hours in the ice bath. White solid. Yield 70%, mp 218-220 °C. ¹H NMR (400 MHz, DMSO-*d*₆): δ = 3.20 (s, 3H, CH₃-N); 4.00 (s, 3H, CH₃-O); 7.94 (s, 1H, NH₂); 8.95 (s, 1H, NH₂); 9.86 (s, 1H, CHO). ¹³C NMR (100 MHz, DMSO-*d*₆): δ = 26.22 (N-CH₃); 55.59 (O-CH₃); 93.61 (C₅); 158.26 (C₂); 162.20 (C₆); 162.84 (C₄); 187.28 (CHO). IR (KBr) cm⁻¹ 3193 (NH *st*), 1733 (C=O *st*). MS (70 eV) *m/z* (%) 183 (M⁺, 31), 155 (100), 125 (21), 42 (23). HR-MS calc. for C₇H₉N₃O₃ 183.0644 found 183.0665.

***N*-(5-Formyl-1-methyl-2,6-dioxo-1,2,3,6-tetrahydropyrimidin-4-yl)formamide 6g.** 0.155 g of 6-Amino-2-methoxy-3-methylpyrimidin-4(3*H*)-one in 1.5 mL of DMF were added to Vilsmeier's reagent (0.15 mL of POCl₃ in 0.5 mL of DMF) and stirred for 2 hours at 50 °C. The

solution was cooled to room temperature and then poured into crushed ice. The solid obtained was filtered and washed with water. White solid. Yield 86%, mp > 300 °C (248-252 °C, decomposed). ¹H NMR (400 MHz, DMSO-*d*₆): δ = 3.17 (s, 3H, CH₃-N); 11.89 (s, 1H, NH); 9.62 (s, 1H, NH); 8.92 (s, 1H, NH-CHO); 9.82 (s, 1H, CHO). ¹³C NMR (100 MHz, DMSO-*d*₆): δ = 26.06 (N-CH₃); 92.34 (C₅); 162.04 (C₂); 148.61 (C₆); 151.48 (C₄); 163.61 (NH-CHO); 188.53 (CHO). IR (KBr) cm⁻¹ 3181 (NH *st*), 1663 (C=O *st*), 1524 (NH δ). MS (70 eV) *m/z* (%) 197 (M⁺, 30), 169 (26), 141 (100), 111 (61), 68 (83). HR-MS calc. for C₇H₇N₃O₄ 197.0437 found 197.0450.

6-Amino-3-methyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-carbaldehyde 3g. 0.197 g (1 mmol) of **6g** were heated to boiled in 30 mL of aqueous NaOH (0.4 M) for 1 hour. The reaction was left to cool at room temperature and the white solid was filtered. The solid recrystallized from ethanol. Yield 84 %, m.p. > 300°C (bibliographic mp > 300 °C).¹⁷

General procedure for the synthesis of pyrido[2,3-*d*]pyrimidines

6-Aminopyrimidin-5-carboxaldehyde **1**, **5a** and **5b** reacts with equimolecular amounts of acetophenones **7** with catalytic amount of BF₃-Et₂O; the mixture of reaction was heated in bath oil at 160 °C for 30 seconds. The resulting dark brown solution was diluted in ethanol and cooled to room temperature. The resulting precipitated was filtered, washed with ethanol and recrystallized to afford the products **8**, **9** and **10** respectively.

1,3-Dimethyl-7-phenylpyrido[2,3-*d*]pyrimidine-2,4(1*H*, 3*H*)-dione 8a. Yellow solid, recrystallized from ethanol, yield 65%, mp 157–159 °C. ¹H NMR (400 MHz, CDCl₃): δ = 3.49 (s, 3H, N₁-CH₃), 3.82 (s, 3H, N₃-CH₃), 7.51-7.5 (m, 3H, H_{*m*} and H_{*p*}), 7.66 (d, 1H, H₆, *J* = 8.03 Hz), 8.13-8.10 (m, 2H, H_o), 8.49 (d, 1H, H₅, *J* = 8.03 Hz). ¹³C NMR (100 MHz, CDCl₃): δ = 28.4 (N₁-CH₃), 29.4 (N₃-CH₃), 109.3 (C_{4a}), 115.5 (C₆), 127.8 (C_o), 129.3 (C_{*m*}), 131.0 (C_{*p*}), 137.8 (C_{*i*}), 138.6 (C₇), 138.7 (C₅), 151.1 (C₄), 152.0 (C₂), 161.6 (C_{8a}). IR (KBr) cm⁻¹ 1706, 1658, (C=O *st*). MS (70 eV) *m/z* (%) 267 (M⁺, 100), 239 (43), 155 (55). HR-MS calc. for C₁₅H₁₃N₃O₂ 267.1008 found 267.1010. Anal. Calcd for C₁₅H₁₃N₃O₂: C, 67.40; H, 4.90; N, 15.72. Found: C, 67.70; H, 4.86; N, 15.26.

1,3-Dimethyl-7-(4-methylphenyl)pyrido[2,3-*d*]pyrimidine-2,4(1*H*, 3*H*)-dione 8b. Yellow crystalline solid, recrystallized from ethanol and DMF mixture, yield 50 %, mp 175–177 °C. ¹H NMR (400 MHz, CDCl₃): δ = 2.44 (s, 3H, CH₃), 3.49 (s, 3H, N₁-CH₃), 3.80 (s, 3H, N₃-CH₃), 7.31 (d, 2H, H_o, *J* = 8.54 Hz), 7.61 (d, 1H, H₆, *J* = 8.03 Hz), 8.00 (d, 2H, H_{*m*}, *J* = 8.28 Hz), 8.44 (d, 1H, H₅, *J* = 8.28 Hz). ¹³C NMR (100 MHz, CDCl₃): δ = 21.3 (N₁-CH₃), 28.3 (N₃-CH₃), 29.3 (CH₃), 108.8 (C_{4a}), 114.7 (C₆), 127.4 (C_{*m*}), 129.6 (C_o), 134.9 (C_{*i*}), 138.2 (C₅), 141.1 (C_{*p*}), 150.8 (C₄), 151.7 (C₂), 161.3 (C_{8a}). IR (KBr) cm⁻¹ 1704, 1662, (C=O *st*). MS (70 eV) *m/z* (%) 281 (M⁺, 100), 252 (51), 169 (50). HR-MS calc. for C₁₆H₁₅N₃O₂ 281.1164 found 281.1159. Anal. Calcd for C₁₆H₁₅N₃O₂: C, 68.31; H, 5.37; N, 14.94. Found: C, 67.90; H, 4.96; N, 14.76.

7-(4-Methoxyphenyl)-1,3-dimethylpyrido[2,3-*d*]pyrimidine-2,4(1*H*, 3*H*)-dione 8c. White solid, recrystallized from ethanol and DMF mixture, yield 60%, mp 163–165 °C. ¹H NMR (400 MHz, CDCl₃): δ = 3.47 (s, 3H, N₁-CH₃), 3.79 (s, 3H, N₃-CH₃), 3.88 (s, 3H, OCH₃), 7.00 (d, 2H,

H_o, $J = 8.78$ Hz), 7.56 (d, 1H, H₆, $J = 8.28$ Hz), 8.07 (d, 2H, H_m, $J = 8.78$ Hz), 8.41 (d, 1H, H₅, $J = 8.03$ Hz). ¹³C NMR (100 MHz, CDCl₃): $\delta = 28.6$ (N₁-CH₃), 29.6 (N₃-CH₃), 55.4 (OCH₃), 108.5 (C_{4a}), 114.3 (C₆), 114.3 (C_m), 129.3 (C_o), 130.3 (C_i), 138.4 (C₅), 151.0 (C₄), 152.0 (C₂), 161.1 (C₇), 161.7 (C_{8a}), 162.2 (C_p). IR (KBr) cm⁻¹ 1702, 1661, (C=O *st*). MS (70 eV) m/z (%) = 297 (M⁺, 100), 268 (35), 185 (31). HR-MS calc. for C₁₆H₁₅N₃O₃ 297.1113 found 297.1114. Anal. Calcd for C₁₆H₁₅N₃O₃: C, 64.64; H, 5.09; N, 14.13. Found: C, 64.26; H, 4.86; N, 14.52.

1,3-Dimethyl-7-(3,4,5-trimethoxyphenyl)pyrido[2,3-*d*]pyrimidine-2,4(1*H*, 3*H*)-dione 8d. Yellow crystalline solid, recrystallized from ethanol and DMF mixture, yield 40%, mp 211–213 °C. ¹H NMR (400 MHz, CDCl₃): $\delta = 3.49$ (s, 3H, N₁-CH₃), 3.81 (s, 3H, N₃-CH₃), 3.93 (s, 3H, C_p-OCH₃), 3.98 (s, 3H, C_m-OCH₃), 7.37 (s, 2H, H_o), 7.60 (d, 1H, H₆, $J = 8.28$ Hz), 8.47 (d, 1H, H₅, $J = 8.28$ Hz). ¹³C NMR (100 MHz, CDCl₃): $\delta = 28.4$ (N₁-CH₃), 29.3 (N₃-CH₃), 56.6 (C_m-OCH₃), 61.3 (C_p-OCH₃), 105.2 (C_o), 109.1 (C_{4a}), 115.2 (C₆), 133.2 (C_i), 138.5 (C₅), 141.0 (C_p), 150.9 (C₄), 151.9 (C₂), 153.9 (C_m), 161.1 (C₇), 161.6 (C_{8a}). IR (KBr) cm⁻¹ 1710, 1655, (C=O *st*). MS (70 eV) m/z (%) 357 (M⁺, 100), 342 (47), 314 (25). HR-MS calc. for C₁₈H₁₉N₃O₅ 357.1325 found 357.1315. Anal. Calcd for C₁₈H₁₉N₃O₅: C, 60.50; H, 5.36; N, 11.76. Found: C, 60.36; H, 5.86; N, 11.92.

7-(1,1'-Biphenyl-4-yl)-1,3-dimethylpyrido[2,3-*d*]pyrimidine-2,4(1*H*, 3*H*)-dione 8e. Yellow solid, purified by column chromatography using chloroform as eluant, yield 60%, mp 233–235 °C. ¹H NMR (400 MHz, CDCl₃): $\delta = 3.49$ (s, 3H, N₁-CH₃), 3.83 (s, 3H, N₃-CH₃), 7.40 (t, 1H, H_p), 7.45 (t, 2H, H_m), 7.65 (d, 2H, H_o, $J = 8.28$ Hz), 7.68 (d, 1H, H₆, $J = 8.03$ Hz), 7.73 (d, 2H, H_m, $J = 8.79$ Hz), 8.19 (d, 2H, H_o, $J = 8.54$ Hz), 8.49 (d, 1H, H₅, $J = 8.03$ Hz). ¹³C NMR (100 MHz, CDCl₃): $\delta = 28.4$ (N₁-CH₃), 29.4 (N₃-CH₃), 109.0 (C_{4a}), 115.0 (C₆), 127.1 (C_o), 127.6 (C_m), 127.9 (C_o), 128.9 (C_m), 136.8 (C_i), 138.3 (C₅), 150.7 (C₄), 151.7 (C₂), 160.9 (C₇), 161.3 (C_{8a}). IR (KBr) cm⁻¹ 1708, 1656, (C=O *st*). MS (70 eV) m/z (%) = 343 (M⁺, 100), 314 (32), 231 (30). HR-MS calc. for C₂₁H₁₇N₃O₂ 343.1321 found 343.1313. Anal. Calcd for C₂₁H₁₇N₃O₂: C, 73.45; H, 4.99; N, 12.24. Found: C, 69.96; H, 5.12; N, 11.96.

7-(4-Hydroxyphenyl)-1,3-dimethylpyrido[2,3-*d*]pyrimidine-2,4(1*H*, 3*H*)-dione 8f. Yellow solid, the residue was washed with hot hexanes, yield 40%, mp >300 °C. ¹H NMR (400 MHz, CDCl₃): $\delta = 3.25$ (s, 3H, N₁-CH₃), 3.59 (s, 3H, N₃-CH₃), 6.87 (d, 2H, H_m, $J = 8.53$ Hz), 7.71 (d, 1H, H₆, $J = 8.28$ Hz), 8.03 (d, 2H, CH_o, $J = 8.54$ Hz), 8.24 (d, 1H, H₅, $J = 8.28$ Hz). ¹³C NMR (100 MHz, CDCl₃): $\delta = 28.3$ (N₁-CH₃), 29.3 (N₃-CH₃), 107.3 (C_{4a}), 114.4 (C₆), 116.4 (C_m), 127.8 (C_i), 129.5 (C_o), 138.1 (C₅), 150.1 (C₄), 150.8 (C₂), 159.7 (C_p), 159.9 (C₇), 160.2 (C_{8a}). IR (KBr) cm⁻¹ 3179 (OH *st*), 1699, 1633, (C=O *st*). MS (70 eV) m/z (%) 283 (M⁺, 100), 254 (45), 171 (47). HR-MS calc. for C₁₅H₁₃N₃O₃ 283.0957, found 283.0965. Anal. Calcd for C₁₅H₁₃N₃O₃: C, 63.60; H, 4.63; N, 14.83. Found: C, 63.86; H, 4.26; N, 14.82.

1,3-Dimethyl-7-(4-nitrophenyl)pyrido[2,3-*d*]pyrimidine-2,4(1*H*, 3*H*)-dione 8g. Yellow solid, recrystallized from DMF, yield 50%, mp 283–285 °C. ¹H NMR (400 MHz, CDCl₃): $\delta = 3.51$ (s, 3H, N₁-CH₃), 3.83 (s, 3H, N₃-CH₃), 7.71 (d, 1H, H₆, $J = 8.03$ Hz), 8.37–8.26 (dd, 4H, H_{arom}, $J = 9.03$ Hz), 8.58 (d, 1H, H₅, $J = 8.03$ Hz). ¹³C NMR (100 MHz, CDCl₃): $\delta = 28.4$ (N₁-CH₃), 29.5 (N₃-CH₃), 110.4 (C_{4a}), 115.7 (C₆), 124.1 (C_m), 128.3 (C_o), 139.0 (C₅), 143.4 (C_i), 149.2 (C_p),

151.2 (C₄), 151.5 (C₂), 158.7 (C₇), 161.0 (C_{8a}). IR (KBr) cm⁻¹ 1705, 1660, (C=O *st*). MS (70 eV) *m/z* (%) = 312 (M⁺, 13), 200 (8), 28 (43), 18 (100). HR-MS calc. for C₁₅H₁₂N₄O₄ 312.0859 found 312.0852. Anal. Calcd for C₁₅H₁₂N₄O₄: C, 57.69; H, 3.87; N, 17.94. Found: C, 56.92; H, 4.16; N, 16.88.

7-(4-Chlorophenyl)-1,3-dimethylpyrido[2,3-*d*]pyrimidine-2,4(1*H*, 3*H*)-dione 8h. Yellow solid, recrystallized from ethanol and DMF mixture, yield 40%, mp 138-140 °C. ¹H NMR (400 MHz, CDCl₃): δ = 3.48 (s, 3H, N₁-CH₃), 3.79 (s, 3H, N₃-CH₃), 7.46 (d, 2H, H_o, *J* = 9.04 Hz), 7.60 (d, 1H, H₆, *J* = 8.03 Hz), 8.04 (d, 2H, H_m, *J* = 8.78 Hz), 8.48 (d, 1H, H₅, *J* = 8.28 Hz). ¹³C NMR (100 MHz, CDCl₃): δ = 28.8 (N₁-CH₃), 29.7 (N₃-CH₃), 109.5 (C_{4a}), 115.2 (C₆), 128.7 (C_m), 129.2 (C_o), 136.2 (C_i), 137.3 (C_p), 138.5 (C₅), 151.1 (C₄), 151.9 (C₂), 160.2 (C₇), 161.5 (C_{8a}). IR (KBr) cm⁻¹ 1705, 1658, (C=O *st*). MS (70 eV) *m/z* (%) 303/301 (M²⁺/M⁺, 35/100), 273 (17). HR-MS calc. for C₁₅H₁₂ClN₃O₂ 301.0618 found 301.0616. Anal. Calcd for C₁₅H₁₂ClN₃O₂: C, 59.71; H, 4.01; N, 13.93. Found: C, 58.92; H, 3.96; N, 13.88.

7-(4-Bromophenyl)-1,3-dimethylpyrido[2,3-*d*]pyrimidine-2,4(1*H*, 3*H*)-dione 8i. White solid, recrystallized from ethanol and DMF mixture, yield 40%, mp 217.5–219.0 °C. ¹H NMR (400 MHz, CDCl₃): δ = 3.48 (s, 3H, N₁-CH₃), 3.79 (s, 3H, N₃-CH₃), 7.64 – 7.60 (t, 3H, H_o and H₆), 7.97 (d, 2H, H_m, *J* = 8.78 Hz), 8.48 (d, 1H, H₅, *J* = 8.28 Hz). ¹³C NMR (100 MHz, CDCl₃): δ = 28.5 (N₁-CH₃), 29.4 (N₃-CH₃), 109.3 (C_{4a}), 114.9 (C₆), 125.4 (C_i), 129.0 (C_m), 132.2 (C_o), 136.1 (C_p), 138.6 (C₅), 150.2 (C₄), 151.6 (C₂), 160.0 (C₇), 161.2 (C_{8a}). IR (KBr) cm⁻¹ 1705, 1656, (C=O *st*). MS (70 eV) *m/z* (%) 347/345 (M²⁺/M⁺, 93/100), 318/316 (36/34), 234/232 (35/38), 154 (32). HR-MS calc. for C₁₅H₁₂N₃O₂Br 345.0113, found 345.0118. Anal. Calcd for C₁₅H₁₂N₃O₂Br: C, 52.04; H, 3.49; N, 12.14. Found: C, 52.22; H, 3.52; N, 12.48.

7-(4-Fluorophenyl)-1,3-dimethylpyrido[2,3-*d*]pyrimidine-2,4(1*H*, 3*H*)-dione 8j. White solid, recrystallized from ethanol and DMF mixture, yield 60%, mp 207–209 °C. ¹H NMR (400 MHz, CDCl₃): δ = 3.48 (s, 3H, N₁-CH₃), 3.80 (s, 3H, N₃-CH₃), 7.18 (t, 2H, H_m), 7.59 (d, 1H, H₆, *J* = 8.03 Hz), 8.11 (m, 2H, H_o), 8.48 (d, 1H, H₅, *J* = 8.03 Hz). ¹³C NMR (100 MHz, CDCl₃): δ = 28.4 (N₁-CH₃), 29.4 (N₃-CH₃), 108.9 (C_{4a}), 114.8 (C₆), 116.1 (C_m), 129.5 (C_o), 138.5 (C₅), 150.7 (C₄), 151.6 (C₂), 160.1 (C₇), 161.3 (C_{8a}), 163.2 (C_i), 165.7 (C_p). IR (KBr) cm⁻¹ 1710, 1668, (C=O *st*). MS (70 eV) *m/z* (%) 285 (M⁺, 100), 257 (43), 173 (54). HR-MS calc. for C₁₅H₁₂N₃O₂F 285.0914 found 285.0913. Anal. Calcd for C₁₅H₁₂N₃O₂F: C, 63.15; H, 4.24; N, 14.73. Found: C, 62.92; H, 4.46; N, 14.38.

1,3-Dimethyl-7-(2-oxo-2*H*-chromen-3-yl)pyrido[2,3-*d*]pyrimidine-2,4(1*H*, 3*H*)-dione 8k. Brown solid, recrystallized from DMF, yield 60%, mp 284.5–286.0 °C ¹H NMR (400 MHz, CDCl₃): δ = 3.51 (s, 3H, N₁-CH₃), 3.82 (s, 3H, N₃-CH₃), 7.38 – 7.33 (m, 2H, H_{aryl}), 7.63 (t, 1H, H_{aryl}), 7.71 (d, 1H, H_{aryl}, *J* = 7.78 Hz), 8.52 – 8.41 (dd, 2H, H₅ and H₆, *J* = 8.03 Hz), 8.85 (s, 1H, CH). ¹³C NMR (100 MHz, CDCl₃): δ = 28.1 (N₁-CH₃), 29.1 (N₃-CH₃), 110.0 (C_{4a}), 116.2 (C_{aryl}), 118.6 (C₆), 118.7 (C_q), 123.5 (C_{q-aryl}), 124.8 (CH_{aryl}), 129.0 (CH_{aryl}), 133.0 (CH_{aryl}), 138.6 (C₅), 144.4 (CH), 150.0 (C₇), 151.2 (C₂), 154.0 (C₄), 154.8 (C_{q-aryl}), 159.3 (C=O), 160.7 (C_{8a}). IR (KBr) cm⁻¹ 1714, 1660, (C=O *st*). MS (70 eV) *m/z* (%) = 335 (M⁺, 100), 306 (47), 223 (56), 195

(20). HR-MS calc. For $C_{18}H_{13}N_3O_4$ 335.0906 found 335.0906. Anal. Calcd for $C_{18}H_{13}N_3O_4$: C, 64.47; H, 3.91; N, 12.53. Found: C, 64.12; H, 4.06; N, 12.48.

3-Methyl-2-(methylthio)-7-phenylpyrido[2,3-*d*]pyrimidin-4(3*H*)-one 9a. Yellow solid, purified by column chromatography using chloroform as eluant, yield 75%, mp 129–131 °C. 1H NMR (400 MHz, $CDCl_3$): δ = 2.69 (s, 3H, SCH_3), 3.51 (s, 3H, CH_3), 7.52–7.55 (m, 3H, H_m , H_p), 8.02 (d, 1H, H_6 , J = 8.28 Hz), 8.19 (d, 2H, H_o , J = 8.28 Hz), 8.49 (d, 1H, H_5 , J = 8.20 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 15.1 (SCH_3), 30.5 (NCH_3), 112.8 (C_{4a}), 118.5 (C_6), 128.0 (C_o), 129.3 (C_m), 130.8 (C_p), 137.7 (C_5), 138.0 (C_i), 156.5 (C_{8a}), 161.2 (C_4), 162.1 (C_2), 162.8 (C_7). IR (KBr) cm^{-1} 3070 (CH *st*), 1682, (C=O *st*). MS (70 eV) m/z (%) 283 (M^+ , 66), 239 (25), 238 (100), 237 (27), 209 (31), 208 (32), 196 (17), 140 (29). HR-MS calc. for $C_{15}H_{13}N_3OS$ 283.0779, found 283.0785. Anal. Calcd for $C_{15}H_{13}N_3OS$: C, 63.58; H, 4.62; N, 14.83. Found: C, 63.88; H, 4.51; N, 14.78.

3-Methyl-2-(methylthio)-7-*p*-tolylpyrido[2,3-*d*]pyrimidin-4(3*H*)-one 9b. Yellow solid, purified by column chromatography using chloroform as eluant, yield 70%, mp 189–191 °C. 1H NMR (400 MHz, $DMSO-d_6$): δ = 2.37 (s, 3H, SCH_3), 2.50 (s, 3H, CH_3), 3.25 (s, 3H, NCH_3), 7.35 (d, 2H, H_m , J = 8.28 Hz), 7.81 (d, 1H, H_6 , J = 8.28 Hz), 8.05 (d, 2H, H_o , J = 8.28 Hz), 8.31 (d, 1H, H_5 , J = 8.28 Hz). ^{13}C NMR (100 MHz, $DMSO-d_6$): δ = 21.4 (SCH_3), 27.6 (CH_3), 40.0 (NCH_3), 108.0 (C_{4a}), 115.5 (C_6), 127.7 (C_o), 130.0 (C_m), 134.6 (C_i), 138.1 (C_5), 140.9 (C_p), 151.1 (C_7), 160.9 (C_4), 162.1 (C_2). IR (KBr) cm^{-1} 3235 (CH *st*), 1716, (C=O *st*). MS (70 eV) m/z (%) 297 (M^+ , 89), 282 (14), 253 (26), 252 (100), 223 (24), 222 (25), 210 (18), 181 (17), 154 (11), 127 (11), 115 (12), 69 (11). HR-MS calc. for $C_{16}H_{15}N_3OS$ 297.0936 found 297.0935. Anal. Calcd for $C_{16}H_{15}N_3OS$: C, 64.62; H, 5.08; N, 14.13. Found: C, 64.50; H, 4.99; N, 13.88.

7-(4-Methoxyphenyl)-3-methyl-2-(methylthio)pyrido[2,3-*d*]pyrimidin-4(3*H*)-one 9c. Yellow solid, purified by washing with hot hexanes, yield 70%, mp 196–198 °C. 1H NMR (400 MHz, $DMSO-d_6$, 373 K): δ = 2.72 (s, 3H, SCH_3), 3.53 (s, 3H, CH_3); 3.86 (s, 3H, OCH_3), 7.08 (d, 2H, H_o , J = 8.68 Hz), 7.89 (d, 1H, H_6 , J = 8.27 Hz), 8.11 (d, 2H, H_m , J = 8.69 Hz), 8.43 (d, 1H, H_5 , J = 8.27 Hz). ^{13}C NMR (100 MHz, $DMSO-d_6$, 373 K): δ = 14.1 (SCH_3), 29.6 (NCH_3), 54.9 (OCH_3), 111.2 (C_{4a}), 113.9 (C_o), 116.8 (C_6), 128.5 (C_m), 129.8 (C_i), 136.3 (C_5), 155.7 (C_{8a}), 160.4 (C_4), 160.9 (C_7), 161.0 (C_2), 161.6 (C_p). IR (KBr) cm^{-1} 1677, (C=O *st*). MS (70 eV) m/z (%) 313 (M^+ , 100), 298 (15), 269 (26), 268 (87), 267 (54), 239 (214), 238 (27), 226 (20), 197 (19). HR-MS calc. for $C_{16}H_{15}N_3O_2S$ 313.0885 found 313.0884. Anal. Calcd for $C_{16}H_{15}N_3O_2S$: C, 61.32; H, 4.82; N, 13.41. Found: C, 61.50; H, 4.59; N, 13.58.

7-(3,4,5-Trimethoxyphenyl)-3-methyl-2-(methylthio)pyrido[2,3-*d*]pyrimidin-4(3*H*)-one 9d. Yellow solid, purified by washing with hot hexanes, yield 70%, mp 211–213 °C. 1H NMR (400 MHz, $DMSO-d_6$): δ = 2.72 (s, 3H, SCH_3), 3.52 (s, 3H, CH_3); 3.76 (s, 3H, OCH_3), 3.93 (s, 6H, OCH_3), 7.48 (s, 2H, H_o), 8.08 (d, 1H, H_6 , J = 8.48 Hz), 8.47 (d, 1H, H_5 , J = 8.27 Hz). ^{13}C NMR (100 MHz, $DMSO-d_6$): δ = 14.8 (SCH_3), 30.1 (NCH_3), 56.1 (OCH_3), 60.2 (OCH_3), 105.0 (C_o), 112.2 (C_{4a}), 118.4 (C_6), 132.8 (C_i), 137.2 (C_5), 139.8 (C_p), 153.2 (C_m), 155.9 (C_{8a}), 160.8 (C_7), 161.1 (C_4), 162.5 (C_2). IR (KBr) cm^{-1} 1679, (C=O *st*). MS (70 eV) m/z (%) 373 (M^+ , 100), 372 (30), 358 (37), 327 (48), 312 (30), 299 (34), 142 (20), 128 (26), 88 (43), 44 (31). HR-MS calc.

for C₁₈H₁₉N₃O₄S 373.1096 found 373.1084. Anal. Calcd for C₁₈H₁₉N₃O₄S: C, 57.89; H, 5.13; N, 11.25. Found: C, 57.54; H, 4.96; N, 11.49.

7-(1,1'-Biphenyl-4yl)-3-methyl-2-(methylthio)pyrido[2,3-d]pyrimidin-4(3H)-one 9e. Yellow solid, purified by column chromatography using chloroform as eluant, yield 50%, mp 222-224 °C. ¹H NMR (400 MHz, CDCl₃): δ = 2.81 (s, 3H, SCH₃), 3.63 (s, 3H, NCH₃), 7.38 (t, 1H, H_p, *J* = 7.28 Hz), 7.47 (t, 2H, H_m, *J* = 7.53 Hz), 7.66 (d, 2H, H_o, *J* = 7.28 Hz), 7.83 (d, 1H, H₆, *J* = 8.28 Hz), 7.74 (d, 2H, H_m, *J* = 8.28 Hz), 8.24 (d, 2H, H_o, *J* = 8.28 Hz), 8.60 (d, 1H, H₅, *J* = 8.03 Hz). ¹³C NMR (100 MHz, CDCl₃): δ = 15.0 (SCH₃), 30.1 (NCH₃), 112.3 (C_{4a}), 118.0 (C₆), 126.8 (C_o), 127.2 (C_o), 127.5 (C_p), 128.1 (C_m), 128.6 (C_m), 136.7 (C_i), 137.2 (C₅), 140.0 (C_i), 142.7 (C_p), 156.6 (C_{8a}), 161.6 (C₂), 162.7 (C₇), 185.3 (C₄). IR (KBr) cm⁻¹ 2922 (CH, *st*), 1676 (C=O *st*). MS (70 eV) *m/z* (%) = 359 (M⁺, 100), 314 (91), 284 (24), 243 (21). HR-MS calc. for C₂₁H₁₇N₃OS 359.1092, found 359.1094. Anal. Calcd for C₂₁H₁₇N₃OS: C, 70.17; H, 4.77; N, 11.69. Found: C, 68.99; H, 4.56; N, 11.29.

7-(4-Hydroxyphenyl)-3-methyl-2-(methylthio)pyrido[2,3-d]pyrimidin-4(3H)-one 9f. Yellow solid, yield 80%, mp 249–251 °C. ¹H NMR (400 MHz, CDCl₃): δ = 2.68 (s, 3H, SCH₃), 3.49 (s, 3H, CH₃); 6.91 (d, 2H, H_m, *J* = 8.53 Hz), 7.91 (d, 1H, H₆, *J* = 8.28 Hz), 8.06 (d, 2H, H_o, *J* = 8.53 Hz), 8.43 (d, 1H, H₅, *J* = 8.29 Hz). ¹³C NMR (100 MHz, CDCl₃): δ = 15.3 (SCH₃), 30.6 (NCH₃), 111.8 (C_{4a}), 116.2 (C_m), 117.8 (C₆), 129.9 (C_o), 137.9 (C₅), 156.3 (C_{8a}), 160.5 (C₄), 161.1 (C₇), 161.6 (C₂), 162.9 (C_p). IR (KBr) cm⁻¹ 3228 (OH, *st*), 1598, (C=O *st*). MS (70 eV) *m/z* (%) 299 (M⁺, 100), 255 (28), 254 (97), 253 (49), 225 (32), 224 (35), 212 (27), 183 (26). HR-MS calc. for C₁₅H₁₃N₃O₂S 299.0728, found 299.0734. Anal. Calcd for C₁₅H₁₃N₃O₂S: C, 60.18; H, 4.38; N, 14.04. Found: C, 60.58; H, 4.48; N, 14.34.

3-Methyl-2-(methylthio)-7-(4-nitrophenyl)pyrido[2,3-d]pyrimidin-4(3H)-one 9g. Yellow solid, recrystallized from DMF, yield 70%, mp 272-274 °C. ¹H NMR (400 MHz, DMSO-*d*₆): δ = 2.74 (s, 3H, SCH₃), 3.56 (s, 3H, CH₃), 8.10 (d, 1H, H₆, *J* = 8.03 Hz), 8.35 (d, 2H, H_o, *J* = 8.79 Hz), 8.45 (d, 2H, H_m, *J* = 8.79 Hz), 8.58 (d, 1H, H₅, *J* = 8.03 Hz). ¹³C NMR (100 MHz, DMSO-*d*₆): δ = 15.3 (SCH₃), 30.6 (NCH₃), 113.7 (C_{4a}), 119.3 (C₆), 124.4 (C_m), 129.1 (C_o), 138.2 (C₅), 143.7 (C_i), 148.8 (C_p), 156.5 (C_{8a}), 159.5 (C₄), 161.2 (C₂), 163.4 (C₇). IR (KBr) cm⁻¹ 3120 (CH *st*), 1675, (C=O *st*). MS (70 eV) *m/z* (%) 328 (M⁺, 54), 313 (12), 284 (26), 283 (100), 254 (21), 253 (18), 166 (11), 97 (15), 69 (20), 43 (17). HR-MS calc. for C₁₅H₁₂N₄O₃S 328.0630 found 328.0617. Anal. Calcd for C₁₅H₁₂N₄O₃S: C, 54.87; H, 3.68; N, 17.06. Found: C, 54.32; H, 3.76; N, 17.22.

7-(4-Chlorophenyl)-3-methyl-2-(methylthio)pyrido[2,3-d]pyrimidin-4(3H)-one 9h. Yellow solid, was recrystallized from a mixture of ethanol – DMF, yield 70%, mp 219.0 – 221.0 °C. ¹H NMR (400 MHz, CDCl₃): δ = 2.70 (s, 3H, SCH₃), 3.52 (s, 3H, CH₃); 7.53 (d, 2H, CH_o, *J* = 8.53 Hz), 7.91 (d, 1H, H₆, *J* = 8.29 Hz), 8.15 (d, 2H, CH_m, *J* = 8.53 Hz), 8.47 (d, 1H, H₅, *J* = 8.29 Hz). ¹³C NMR (100 MHz, CDCl₃): δ = 14.5 (SCH₃), 30.0 (CH₃), 112.3 (C_{4a}), 117.7 (C₆), 128.6 (C_o), 129.0 (C_m), 135.2 (C_i), 136.4 (C_p), 137.1 (C₅), 156.0 (C_{8a}), 160.4 (C₄), 160.8 (C₇), 162.3 (C₂). IR (KBr) cm⁻¹ 1687, (C=O *st*). MS (70 eV) *m/z* (%) 319/317 (M²⁺/M⁺, 22/58), 274/272 (35/100), 271 (26), 243 (24), 232/230 (5/15), 166/165 (19/5). HR-MS calc. for C₁₅H₁₂ClN₃OS 317.0390

found 317.0399. Calcd for C₁₅H₁₂ClN₃OS: C, 56.69; H, 3.81; N, 13.22. Found: C, 56.22; H, 3.86; N, 13.12.

7-(4-Bromophenyl)-3-methyl-2-(methylthio)pyrido[2,3-*d*]pyrimidin-4(3*H*)-one 9i. Yellow solid, purified by washing with hot hexanes, yield 80%, mp 206–208 °C. ¹H NMR (400 MHz, DMSO-*d*₆): δ = 2.68 (s, 3H, SCH₃), 3.50 (s, 3H, CH₃); 7.73 (d, 2H, H_o, *J* = 8.29 Hz), 8.02 (d, 1H, H₆, *J* = 8.28 Hz), 8.15 (d, 2H, H_m, *J* = 8.54 Hz), 8.48 (d, 1H, H₅, *J* = 8.29 Hz). ¹³C NMR (100 MHz, DMSO-*d*₆): δ = 15.3 (SCH₃), 30.7 (CH₃), 113.1 (C_{4a}), 118.4 (C₆), 124.7 (C_p), 129.9 (C_o), 132.4 (C_m), 137.1 (C_i), 137.9 (C₅), 156.6 (C_{8a}), 160.7 (C₂), 161.3 (C₇), 163.0 (C₄). IR (KBr) cm⁻¹ 1689, (C=O *st*). MS (70 eV) *m/z* (%) 363/361 (M⁺²/M⁺, 54/54), 317/315 (93/100), 288/286 (19/20), 246/244 (19/15). HR-MS calc. for C₁₅H₁₂BrN₃OS 360.9884, found 360.8978. Anal. Calcd for C₁₅H₁₂BrN₃OS: C, 49.73; H, 3.34; N, 11.60. Found: C, 51.12; H, 3.45; N, 11.44.

7-(4-Fluorophenyl)-3-methyl-2-(methylthio)pyrido[2,3-*d*]pyrimidin-4(3*H*)-one 9j. Yellow solid, purified by column chromatography using chloroform as eluant, yield 70%, mp 202–204 °C. ¹H NMR (400 MHz, DMSO-*d*₆): δ = 2.69 (s, 3H, SCH₃), 3.51 (s, 3H, CH₃); 7.36 (t, 2H, H_m, *J* = 8.78 Hz), 8.02 (d, 1H, H₆, *J* = 8.28 Hz), 8.25–8.29 (m, 2H, H_o), 8.48 (d, 1H, H₅, *J* = 8.29 Hz). ¹³C NMR (100 MHz, DMSO-*d*₆): δ = 15.2 (SCH₃), 30.6 (CH₃), 112.7 (C_{4a}), 116.4 (C_o), 118.3 (C₆), 130.2 (C_m), 134.5 (C_p), 137.8 (C₅), 156.6 (C_{8a}), 160.9 (C₄), 161.3 (C₂), 162.8 (C₇). IR (KBr) cm⁻¹ 1664 (C=O *st*). MS (70 eV) *m/z* (%) 301 (M⁺, 74), 271 (16), 257 (27), 256 (100), 255 (31), 227 (29), 226 (31), 214 (23), 185 (20), 158 (29). HR-MS calc. for C₁₅H₁₂FN₃OS 301.0685, found 301.0688. Anal. Calcd for C₁₅H₁₂FN₃OS: C, 59.79; H, 4.01; N, 13.94. Found: C, 59.12; H, 4.12; N, 13.06.

3-Methyl-2-(methylthio)-7-(2-oxo-2*H*-chromen-3-yl)pyrido[2,3-*d*]pyrimidin-4(3*H*)-one 9k. Yellow solid, yield 70%, recrystallized from ethanol, mp 217–219 °C. ¹H NMR (400 MHz, CDCl₃): δ = 2.79 (s, 3H, SCH₃), 3.64 (s, 3H, NCH₃), 7.34 (t, 1H, H_{aryl}), 7.38 (d, 1H, H_{aryl}, *J* = 8.29 Hz), 7.59 (t, 1H, H_{aryl}), 7.68 (d, 2H, H_{aryl}, *J* = 7.65 Hz), 8.47 (d, H₆, *J* = 8.28 Hz), 8.61 (d, H₅, *J* = 8.28 Hz), 9.00 (s, 1H, CH). ¹³C NMR (100 MHz, CDCl₃): δ = 15.3 (SCH₃), 30.5 (NCH₃), 113.7 (C_{4a}), 116.5 (C₆), 119.2 (C_q), 121.6 (C_{aryl}), 121.6 (C_{aryl}), 124.2 (C_{q-aryl}), 124.8 (C_{aryl}), 129.3 (C_{aryl}), 133.0 (C_{aryl}), 137.8 (C₅), 145.4 (CH), 154.3 (C₇), 156.3 (C₂), 157.4 (C₄), 160.8 (C_{q-aryl}), 161.5 (C=O), 163.1 (C_{8a}). IR (KBr) cm⁻¹ 1729, 1681, (C=O *st*). MS (70 eV) *m/z* (%) 353 (M⁺, 5), 352 (16), 351 (79), 336 (14), 307 (25), 306 (100), 277 (32), 275 (22), 264 (14). HR-MS calc. for C₁₈H₁₃N₃O₃S 351.0678, found 351.0683. Anal. Calcd for C₁₈H₁₃N₃O₃S: C, 61.53; H, 3.73; N, 11.96. Found: C, 59.96; H, 3.92; N, 13.14.

3-Methyl-7-phenylpyrido[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione 10a. White solid, yield 70%, m.p 291–293 °C. ¹H NMR (400 MHz, DMSO-*d*₆): δ = 3.25 (s, 3H, NCH₃), 7.51–7.55 (m, 3H, H_m, H_p), 7.82 (d, 1H, H₆, *J* = 8.03 Hz), 8.13 (d, 2H, H_o, *J* = 7.79 Hz), 8.33 (d, 1H, H₅, *J* = 8.28 Hz), 11.96 (s, 1H, NH). ¹³C NMR (100 MHz, DMSO-*d*₆): δ = 27.5 (NCH₃), 108.4 (C_{4a}), 115.8 (C₆), 127.7 (C_o), 129.3 (C_m), 130.9 (C_p), 137.4 (C_i), 138.1 (C₅), 151.1 (C-7), 151.2 (C_{8a}), 160.9 (C₄), 162.0 (C₂). IR (KBr) cm⁻¹ 3150 (NH, *st*), 1726 (C=O *st*). The mass spectrum shows the following peaks: MS (70 eV) *m/z* (%) = 253 (M⁺, 100), 224 (24), 196 (33), 169 (26), 140 (19). HRMS calc.

for C₁₄H₁₁N₃O₂ 253.0851, found 253.0856. Anal. Calcd for C₁₄H₁₁N₃O₂: C, 66.40; H, 4.38; N, 16.59. Found: C, 66.78; H, 4.56; N, 16.52.

3-Methyl-7-*p*-tolylpyrido[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione 10b. White solid, yield 60%, m.p. > 300 °C. ¹H NMR (400 MHz, DMSO-*d*₆, 393 K): δ = 2.38 (s, 3H, CH₃), 3.29 (s, 3H, NCH₃), 7.31 (d, 2H, H_o, *J* = 8.00 Hz), 7.70 (d, 1H, H₆, *J* = 8.28 Hz), 8.00 (d, 2H, H_m, *J* = 8.00 Hz), 8.29 (d, 1H, H₅, *J* = 8.28 Hz), 11.32 (s, 1H, NH). ¹³C NMR (100 MHz, DMSO-*d*₆, 393 K): δ = 20.1 (CH₃), 26.2 (NCH₃), 107.0 (C_{4a}), 114.4 (C₆), 126.6 (C_m), 128.7 (C_o), 134.1 (C_i), 136.8 (C₅), 139.6 (C_p), 150.0 (C-7), 160.4 (C₄), 161.1 (C₂), 150.1 (C_{8a}). IR (KBr) cm⁻¹ 3122 (NH, *st*), 1712 (C=O *st*). MS (70 eV) *m/z* (%) 267 (M⁺, 100), 238 (16), 210 (26), 183 (17). HRMS calc. For C₁₅H₁₃N₃O₂ 267.1008 found 267.1009. Anal. Calcd for C₁₅H₁₃N₃O₂: C, 67.40; H, 4.90; N, 15.72. Found: C, 66.96; H, 4.52; N, 15.76.

7-(4-Methoxyphenyl)-3-methylpyrido[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione 10c. Yellow solid, recrystallized from DMF, yield 70%, mp >300 °C. ¹H NMR (400 MHz, DMSO-*d*₆): δ = 3.24 (s, 3H, NCH₃), 3.83 (s, 3H, OCH₃), 7.57 (d, 2H, H_m, *J* = 8.78 Hz), 7.75 (d, 1H, H₆, *J* = 8.28 Hz), 8.12 (d, 2H, H_o, *J* = 7.53 Hz), 8.26 (d, 1H, H₅, *J* = 8.28 Hz), 11.68 (s, 1H, NH). ¹³C NMR (100 MHz, DMSO-*d*₆): δ = 26.5 (NCH₃), 55.8 (OCH₃), 107.1 (C_{4a}), 114.8 (C_o), 115.0 (C₆), 129.4 (C_m), 129.5 (C_i), 137.9 (C₅), 149.8 (C₇), 150.7 (C_{8a}), 155.8 (C_p), 160.2 (C₄), 161.3 (C₂). IR (KBr) cm⁻¹ 3280, (NH *st*), 1720, (C=O *st*). MS (70 eV) *m/z* (%) 283 (M⁺, 100), 254 (10), 226 (20), 155 (8). HR-MS calc. for C₁₅H₁₃N₃O₃ 283.0957, found 283.0966. Anal. Calcd for C₁₅H₁₃N₃O₃: C, 63.60; H, 4.63; N, 14.83. Found: C, 64.06; H, 4.53; N, 14.95.

7-(3,4,5-Trimethoxyphenyl)-3-methylpyrido[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione 10d. Brown solid, recrystallized from DMF, yield 60%, mp 297-299 °C. ¹H NMR (400 MHz, DMSO-*d*₆): δ = 3.24 (s, 3H, NCH₃), 3.73 (s, 3H, OCH₃), 3.88 (s, 6H, OCH₃), 7.46 (s, 2H, H_o), 7.86 (d, 1H, H₆, *J* = 8.28 Hz), 8.28 (d, 1H, H₅, *J* = 8.28 Hz), 11.90 (s, 1H, NH). ¹³C NMR (100 MHz, DMSO-*d*₆): δ = 27.6 (NCH₃), 56.5 (C_m-OCH₃), 60.6 (C_p-OCH₃), 105.3 (C_o), 108.1 (C_{4a}), 115.8 (C₆), 132.8 (C_i), 137.9 (C₅), 140.3 (C_p), 151.0 (C₇), 151.1 (C_{8a}), 153.6 (C_m), 160.2 (C₄), 162.1 (C₂). IR (KBr) cm⁻¹ 3053, (NH *st*), 1715, (C=O *st*). MS (70 eV) *m/z* (%) 343 (M⁺, 100), 328 (46), 270 (22), 213 (17), 257 (17). HR-MS calc. for C₁₇H₁₇N₃O₅ 343.1168, found 343.1169. Anal. Calcd for C₁₇H₁₇N₃O₅: C, 59.47; H, 4.99; N, 12.24. Found: C, 58.19; H, 5.03; N, 13.07.

7-(1,1'-Biphenyl-4-yl)-3-methylpyrido[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione 10e. Yellow solid, yield 40%, mp >300 °C. ¹H NMR (400 MHz, DMSO-*d*₆, 393 K): δ = 3.30 (s, 3H, NCH₃), 7.38 (t, 1H, H_p), 7.71–7.52 (m, 7H, H_{arom}), 8.22 (d, 2H, H_{arom}, *J* = 8.69 Hz), 8.35 (d, 1H, H₅, *J* = 8.07 Hz), 11.38 (s, 1H, NH). ¹³C NMR (100 MHz, DMSO-*d*₆, 393 K): δ = 26.3 (NCH₃), 114.7 (C₆), 126.0 (C_o), 126.4 (C_o), 127.1 (C_p), 127.2 (C_m), 128.2 (C_m), 136.9 (C₅), 141.7 (C_q), 142.2 (C_q), 149.9 (C₇), 150.2 (C_{8a}), 152.1 (C₂). IR (KBr) cm⁻¹ 3452 (NH, *st*), 1724 (C=O *st*). MS (70 eV) *m/z* (%) 329 (M⁺, 100), 300 (11), 272 (19), 246 (10). HR-MS calc. for C₂₀H₁₅N₃O₂ 329.1164, found 329.1165. Anal. Calcd for C₂₀H₁₅N₃O₂: C, 72.94; H, 4.59; N, 12.76. Found: C, 72.56; H, 4.66; N, 12.50.

7-(4-Hydroxyphenyl)-3-methylpyrido[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione 10f. Yellow solid, recrystallized from DMF, yield 60%, mp >300 °C. ¹H NMR (400 MHz, DMSO-*d*₆): δ = 3.24 (s,

3H, NCH₃), 6.89 (d, 2H, H_m, *J* = 8.28 Hz), 7.70 (d, 1H, H₆, *J* = 8.28 Hz), 8.02 (d, 2H, H_o, *J* = 8.78 Hz), 8.24 (d, 1H, H₅, *J* = 8.28 Hz), 11.84 (s, 1H, NH). ¹³C NMR (100 MHz, DMSO-*d*₆): δ = 26.5 (NCH₃), 107.2 (C_{4a}), 116.1 (C_o), 114.7 (C₆), 129.5 (C_m), 128.3 (C_i), 137.8 (C₅), 150.2 (C₇), 151.2 (C_{8a}), 161.1 (C₄), 162.1 (C₂), 163.6 (C_p). IR (KBr) cm⁻¹ 3362 (OH *st*), 3257 (NH *st*), 1720-1666 (C=O *st*). MS (70 eV) *m/z* (%) 269 (M⁺, 2), 169 (32), 141 (100), 110 (20), 84 (29), 68 (22), 43 (17). HR-MS calc. for C₁₄H₁₁N₃O₃ 269.0728 found 269.0730. Anal. Calcd for C₁₄H₁₁N₃O₃: C, 62.45; H, 4.12; N, 15.61. Found: C, 61.96; H, 4.26; N, 15.85.

7-(4-Chlorophenyl)-3-methylpyrido[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione 10h. Yellow solid, purified by washing with hot hexanes, yield 60%, mp 313–315 °C. ¹H NMR (400 MHz, CDCl₃): δ = 3.22 (s, 3H, NCH₃), 7.56 (broad band, 2H, H_m), 7.78 (broad band, 1H, H₆), 8.11 (broad band, 2H, H_o), 8.29 (broad band, 1H, H₅), 11.95 (s, 1H, NH). ¹³C NMR (100 MHz, CDCl₃): δ = 27.5 (NCH₃), 108.7 (C_{4a}), 115.8 (C₆), 125.0 (C_o), 129.3 (C_m), 136.0 (C_i), 136.5 (C_p), 138.3 (C₅), 151.0 (C_{8a}), 151.2 (C₄), 162.0 (C₂), 160.0 (C₇). IR (KBr) cm⁻¹ 3230, (NH *st*), 1722, (C=O *st*). MS (70 eV) *m/z* (%) 287(M⁺, 100), 289/287(M⁺²/M⁺, 33/100), 258/256(20/6), 230(30), 203/201 (25/6), 140 (43). HR-MS calc. for C₁₄H₁₀ClN₃O₂ 287.0462 found 287.0459. Anal. Calcd for C₁₄H₁₀ClN₃O₂: C, 58.45; H, 3.50; N, 14.61. Found: C, 58.86; H, 3.46; N, 14.85.

7-(4-Bromophenyl)-3-methylpyrido[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione 10i. Pink solid, recrystallized from ethanol, yield 50%, mp 310-312 °C dec. ¹H NMR (400 MHz, CDCl₃): δ = 3.47 (s, 3H, NCH₃), 7.59 – 7.64 (m, 3H, H_m, H₆), 7.92 (d, 2H, H_o, *J* = 7.53 Hz), 8.12 (s, 1H, NH), 8.45 (d, 1H, H₅, *J* = 8.03 Hz). ¹³C NMR (100 MHz, CDCl₃): δ = 27.5 (OCH₃), 99.7 (C_{4a}), 115.7 (C₆), 128.7 (C_m), 131.9 (C_o), 138.3 (C₅). IR (KBr) cm⁻¹ 3193 (NH *st*), 1733 (C=O *st*). MS (70 eV) *m/z* (%) 332/330 (M⁺²/M⁺, 97/100), 303/301(15/15), 275/273(25/23), 248/246(20/22), 140 (72). HR-MS calc. for C₁₄H₁₀BrN₃O₂ 330.9956 found 330.9970. Anal. Calcd for C₁₄H₁₀BrN₃O₂: C, 50.62; H, 3.03; N, 12.65. Found: C, 50.22; H, 3.28; N, 12.74.

7-(4-Fluorophenyl)-3-methylpyrido[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione 10j. Yellow solid, yield 60%, mp 295-297 °C. ¹H NMR (400 MHz, CDCl₃): δ = 3.21 (s, 3H, NCH₃), 7.32 (t, 2H, H_m), 7.75 (d, 1H, H₆, *J* = 8.28 Hz), 8.13 – 8.17 (m, 2H, H_o), 8.27 (d, 1H, H₅, *J* = 8.28 Hz), 11.95 (s, 1H, NH). ¹³C NMR (100 MHz, CDCl₃): δ = 27.6 (NCH₃), 108.3 (C_{4a}), 115.6 (C₆), 116.4 (C_m), 130.1 (C_o), 133.9 (C_i), 138.3 (C₅), 151.2 (C₄), 162.1 (C₂), 162.7 (C_{8a}), 165.8 (C_p). IR (KBr) cm⁻¹ 3222 (NH, *st*), 1717 (C=O *st*). MS (70 eV) *m/z* (%) 271 (M⁺, 100), 242 (19), 214 (22), 187 (19), 158 (18), 69 (27). HR-MS calc. for C₁₄H₁₀FN₃O₂ 271.0757, found 271.0752. Anal. Calcd for C₁₄H₁₀FN₃O₂: C, 61.99; H, 3.72; N, 15.49. Found: C, 61.22; H, 3.46; N, 15.50.

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