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SYNTHESIS OF NOVEL TETRACYCLIC THIENO[3',2':2,3]PYRIDO-[4,5-*d*]PYRIDO[1,2-*a*]PYRIMIDINONES VIA PICTET-SPENGLER CYCLIZATION

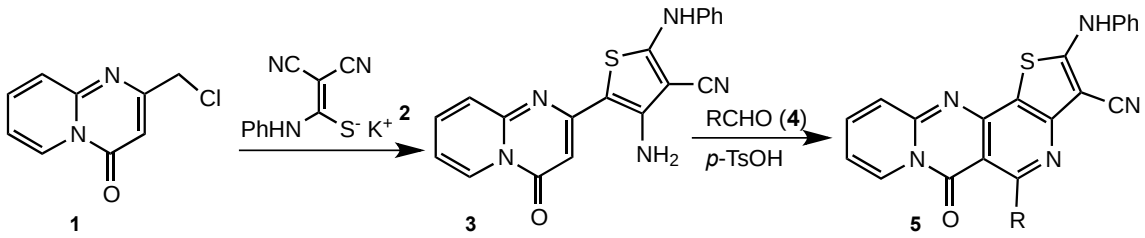
Yi-Xin Tang, Dao-Lin Wang,* and Jian-Hua Qian

Liaoning Key Laboratory of Synthesis & Application of Functional Compound, College of Chemistry & Chemical Engineering, Bohai University, Jinzhou 121001, P. R. China; wangdaolin@sina.com

Abstract – Synthesis of novel thieno[3',2':2,3]pyrido[4,5-*d*]pyrido[1,2-*a*]-pyrimidin-5-one derivatives (**5**) via Pictet-Spengler cyclization is reported. The key intermediate, 2-(3-amino-4-cyano-5-phenylaminothieno-2-yl)-4*H*-pyrido-[1,2-*a*]pyrimidin-4-one (**3**), was readily prepared from 2-chloromethyl-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**1**) with potassium (2,2-dicyano-1-phenylamino-ethen-1-yl)thiolate (**2**) by Thorpe-Ziegler isomerization. Reaction of the intermediate amine with aromatic aldehydes in the presence of *p*-TsOH gives tetracyclic thienopyridine-fused pyrido[1,2-*a*]pyrimidines **5** in good yields.

Nitrogen heterocycles have always attracted much attention in natural products, materials, and pharmaceutical chemistry. The pyrimidine core is a privileged structure in medical chemistry. Moreover, fused pyrimidine systems have been important in drug design over many years due to diverse biological properties.[1] In particular, the 4*H*-pyrido[1,2-*a*]pyrimidin-4-one skeleton is a privileged scaffold in medicinal chemistry, which has shown broad biological activities, such as antipsychotic, antiallergic, antidepressant, as a tranquilizing agent, antihypertensive and antilucerative.[2] For example, this structural pattern is present in the known antiallergic agent ramastine[3] and human leukocyte elastase inhibitor SSR69071.[4] Therefore, search for new biologically active compounds in this series seems to be quite promising. Owing to these remarkably broad pharmacological properties, a variety of synthetic methods have been reported for the preparation of pyrido[1,2-*a*]pyrimidinone derivatives.[5]

As part of our studies on construction of biologically important heterocycles,[6] herein we report the synthesis of some new fused heterocyclic compounds: thieno[3',2':2,3]pyrido[4,5-*d*]pyrido[1,2-*a*]-pyrimidines by the application of Pictet-Spengler reaction (Scheme 1).



Scheme 1. Syntheses of thienopyrido-fused pyridopyrimidines

To access the target thieno[3',2':2,3]pyrido[4,5-*d*]pyrido[1,2-*a*]pyrimidin-5-ones, we envisioned a strategy by which the Pictet-Spengler cyclization key reaction step consists of a condensation reaction of amine **3** with aromatic aldehydes.

The key intermediate amine, 2-(3-amino-4-cyano-5-phenylaminothieno-2-yl)-4*H*-pyrido[1,2-*a*]-pyrimidin-4-one (**3**) was readily obtained by the condensation of 2-chloromethyl-4*H*-pyrido[1,2-*a*]-pyrimidin-4-one (**1**) with potassium (2,2-dicyano-1-phenylaminoethen-1-yl)thiolate (**2**) *via* Thorpe-Ziegler isomerization,[7] in 87% yield. Elemental analysis ($C_{19}H_{13}N_5OS$) and spectral data supported its structure. Its IR spectrum contains absorption peaks at 3429, 3352, 2218 and 1683 cm^{-1}, demonstrating the presence of NH, CN and C=O funcitions, respectively. Its ^1H NMR spectrum (DMSO-d_6) shows the presence of a D_2O exchangeable broad singlet at δ 7.28 (2H) and 10.28 ppm (1H) which can be attributed to the NH_2 and NH protons, respectively. The singlet peak at δ 5.69 corresponding to C_3-H of pyrido[1,2-*a*]pyrimidine nucleus. The multiplet between 7.14-8.81 ppm (9H) corresponding to the aromatic protons of benzene and pyridine nucleus.

In an initial endeavor, we selected benzaldehyde **4a** as model aromatic aldehyde to react with equimolar amounts of intermediate amine **3a** for the preparation of 8-cyano-6-phenyl-9-phenylamino-5*H*-thieno-[3',2':2,3]pyrido[4,5-*d*]pyrido[1,2-*a*]pyrimidin-5-one **5a** and investigated the optimal reaction conditions. The reaction was carried out under neat conditions at 120 °C without and with different acid catalysts such as sulfamic acid (SA), trifluoroacetic acid (TFA), and *p*-toluenesulfonic acid (*p*-TsOH) each 10 mol% in HOAc. The maximum yield was obtained using *p*-TsOH. It can be seen that the reaction did not proceed even after 24 h in the absence of this catalyst (Table 1, entry 1). Although a lower catalyst loading of 5 mol% accomplished this condensation, 10 mol% of *p*-TsOH was optimal in terms of reaction time and isolated yield (Table 1, entry 4). Increasing the amount from 10 to 15 mol% has no effect on the product yield and reaction time (Table 1, entry 6).

In addition, various solvents such as DMF, DMSO, toluene, and MeCN were screened for the optimal reaction conditions. The best catalytic activity was observed in HOAc compared to other organic solvents (Table 1, entries 7-10).

Table 1. Optimization of reaction conditions on the synthesis of **5a**[a]

Entry	Catalyst / (mol%)	Solvent	Temp (°C)	Time (h)	Yield (%)
1	none	HOAc	120	24	Trace
2	SA (10)	HOAc	120	10	60
3	TFA (10)	HOAc	120	7	74
4	*p*-TsOH (10)	HOAc	120	8	83
5	*p*-TsOH (5)	HOAc	120	12	71
6	*p*-TsOH (15)	HOAc	120	8	82
7	*p*-TsOH (10)	DMF	120	12	74
8	*p*-TsOH (10)	DMSO	120	10	63
9	*p*-TsOH (10)	toluene	110	24	37
10	*p*-TsOH (10)	MeCN	80	18	52

* Reaction conditions: **3** (1.0 mmol), benzaldehyde (**4a**, 1.0 mmol), solvent (20 mL).

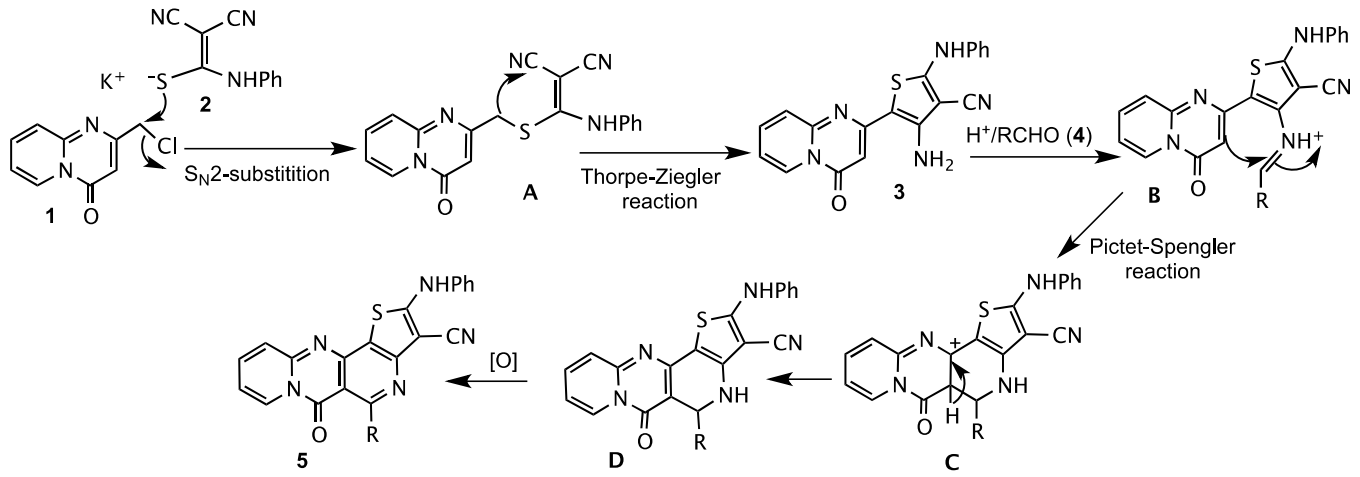
With these optimized reaction conditions in hand, we then planned to examine the versatility of the methodology for the preparation of thienopyridine-fused pyrido[1,2-*a*]pyrimidines. The substrate scope of the *p*-TsOH catalyzed coupling of **1** with aromatic aldehydes **4** is shown in Table 2.

Table 2. Synthesis of thieno[3',2':2,3]pyrido[4,5-*d*]pyrido[1,2-*a*]pyrimidin-5-ones **5**

Entry	**4** / R		Time (h)	Product	Yield (%)
1	**4a**	C_6H_5	8	**5a**	83
2	**4b**	4-MeC_6H_4	7	**5b**	84
3	**4c**	3-$MeOC_6H_4$	7	**5c**	80
4	**4d**	4-$MeOC_6H_4$	6	**5d**	86
5	**4e**	3,4-$(MeO)_2C_6H_3$	6	**5e**	89
6	**4f**	4-HOC_6H_4	8	**5f**	85
7	**4g**	2-FC_6H_4	9	**5g**	76
8	**4h**	4-FC_6H_4	8	**5h**	84
9	**4i**	4-ClC_6H_4	7	**5i**	80
10	**4j**	4-$NO_2C_6H_4$	10	**5j**	75
11	**4k**	2-furyl	11	**5k**	76
12	**4l**	2-thienyl	12	**5l**	81

It was found that this protocol could be applied not only to the aromatic aldehydes with either electron-donating groups (e.g., methyl, methoxy, hydroxy) or electron-withdrawing groups (e.g., fluoro, chloro, and nitro groups), but also to heterocyclic aldehydes. Therefore, we concluded that the electronic nature of the substituents of aldehydes has no significant effect on this reaction.

On the basis of these results, a plausible mechanism for the construction of fused pyrido[1,2-*a*]-pyrimidinones is proposed (Scheme 2). The formation of ether **A** occurs through *S*-alkylation of 2-chloro-methyl-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**1**) and potassium (2,2-dicyano-1-phenylaminoethen-1-yl)-thiolate (**2**). Then, the ether **A** occurred *via* Thorpe-Ziegler isomerization reaction to generate 2-(3-amino-4-cyano-5-phenylaminothieno-2-yl)-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**3**). Next, the intermediate amine **3** underwent a cationic π-cyclization with aldehyde (**4**) under Pictet-Spengler cyclization to form **D**, which effects aromatization to give tetracyclic product **5**.



Scheme 2. Proposed reaction mechanism for the formation of compound **5**

In summary, we have developed an efficient and versatile method for the preparation of thienopyridine-fused pyrido[1,2-*a*]pyrimidine derivatives based on 6,6,6,5-tetracyclic systems using the modified Pictet-Spengler reaction with good yields. This method has the advantages of readily available starting materials, mild reaction conditions, and operational simplicity. Further study is underway to the scope of this methodology for some new fused heterocyclic systems.

EXPERIMENTAL

Melting points were determined in open capillaries and are uncorrected. The NMR spectra were recorded with a Bruker Avance 400 spectrometer (400 MHz for ^{1}H and 100 MHz for ^{13}C) using TMS an internal reference. IR spectra were measured on Shimadzu FTIR-8300 spectrophotometer. C, H and N analyses were performed by a HP-MOD 1106 microanalyzer. The preparation of 2-chloromethyl-4*H*-pyrido-

[1,2-*a*]pyrimidin-4-one (**1**)[8] and potassium (2,2-dicyano-1-phenylaminoethen-1-yl)thiolate (**2**)[9] were according to the literature procedure. All other chemicals used in this study were commercially available.

Preparation of 2-(3-amino-4-cyano-5-phenylaminothieno-2-yl)-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (3): To a solution of 2-chloromethyl-4*H*-pyrido[1,2-*a*]pyrimidin-4-one **1** (1.94 g, 10.0 mmol) in DMF (25 mL) was added potassium (2,2-dicyano-1-phenylaminoethen-1-yl)thiolate **2** (2.39 g, 10.0 mmol) and anhydrous potassium carbonate (2.76 g, 20.0 mmol). The mixture was heated at 100 °C for 6 h (monitored by TLC). After cooling to rt, then water (50 mL) was added and stirred for 20 min. The solid was filtered and recrystallized from HOAc to give **3** (3.12 g, 87%). Yellow crystals. mp > 300 °C; IR (KBr): *v* 3429, 3352 (NH), 2218 (CN), 1683 cm^{-1} (C=O). ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.69 (s, 1H), 7.14-7.20 (m, 2H), 7.28 (s, 2H), 7.43-7.44 (m, 4H), 7.59 (d, J = 8.8 Hz, 1H), 7.83 (t, J = 8.0 Hz, 1H), 8.81 (d, J = 8.4 Hz, 1H), 10.28 (s, 1H). *Anal*. Calcd for $C_{19}H_{13}N_5OS$: C 63.49, H 3.65, N 19.49. Found: C 63.57, H 3.67, N 19.53.

Typical Procedure for the Preparation of 6-Aryl-8-cyano-9-phenylamino-5*H*-thieno[3',2':2,3]-pyrido[4,5-*d*]pyrido[1,2-*a*]pyrimidin-5-ones. To a stirred solution of 2-(3-amino-4-cyano-5-phenyl-aminothieno-2-yl)-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**3**) (360 mg, 1.0 mmol), aromatic aldehyde (1.0 mmol), and *p*-TsOH (20 mg, 0.1 mmol) in HOAc (20 mL) was heated at 120 °C (monitored by TLC). At the end of the reaction, the reaction mixture was cooled to rt, filtered and recrystallized from DMF to afford the corresponding products **5a-l**.

8-Cyano-6-phenyl-9-phenylamino-5*H*-thieno[3',2':2,3]pyrido[4,5-*d*]pyrido[1,2-*a*]pyrimidin-5-one (5a): Yellow crystals. mp > 300 °C; IR (KBr): *v* 3341 (NH), 2207 (CN), 1685 cm^{-1} (C=O). ^{1}H NMR (400 MHz, CF_3CO_2D): δ 7.55-7.56 (m, 5H), 7.62-7.69 (m, 6H), 7.81-7.85 (m, 1H), 8.17 (d, J = 8.6 Hz, 1H), 8.68 (d, J = 8.4 Hz, 1H), 9.25 (s, 1H). ^{13}C NMR (100 MHz, CF_3CO_2D): δ 173.1, 159.9, 151.0, 149.9, 148.2, 147.3, 141.0, 136.4, 132.6, 131.2, 130.5, 130.3, 128.8, 128.8, 127.5, 123.3, 120.9, 117.5, 117.5, 109.2, 102.1, 77.5. *Anal*. Calcd for $C_{26}H_{15}N_5OS$: C 70.10, H 3.39, N 15.72. Found: C 70.17, H 3.41, N 15.73.

8-Cyano-6-(4-methylphenyl)-9-phenylamino-5*H*-thieno[3',2':2,3]pyrido[4,5-*d*]pyrido[1,2-*a*]pyrimi-din-5-one (5b): Yellow crystals. mp > 300 ºC; IR (KBr): *v* 3342 (NH), 2211 (CN), 1688 cm^{-1} (C=O). ^{1}H NMR (400 MHz, CF_3CO_2D): δ 2.57 (s, 3H), 7.53-7.55 (m, 6H), 7.64-7.69 (m, 4H), 7.87-7.88 (m, 1H), 8.17 (d, J = 8.6 Hz, 1H), 8.68 (d, J = 8.4 Hz, 1H), 9.27 (s, 1H). ^{13}C NMR (100 MHz, CF_3CO_2D): δ 173.0, 160.3, 151.1, 149.8, 148.2, 147.2, 144.9, 141.1, 136.4, 131.2, 130.5, 130.2, 129.5, 127.7, 125.8, 123.3, 120.8, 117.5, 109.2, 108.8, 101.9, 77.5, 19.6. *Anal*. Calcd for $C_{27}H_{17}N_5OS$: C 70.57, H 3.73, N 15.24. Found: C 70.63, H 3.76, N 15.28.

8-Cyano-6-(3-methoxyphenyl)-9-phenylamino-5*H*-thieno[3',2':2,3]pyrido[4,5-*d*]pyrido[1,2-*a*]pyri-midin-5-one (5c): Yellow crystals. mp > 300 ºC; IR (KBr): *v* 3348 (NH), 2209 (CN), 1683 cm^{-1} (C=O).

^{1}H NMR (400 MHz, CF_3CO_2D): δ 3.99 (s, 3H), 7.21-7.26 (m, 4H), 7.38-7.46 (m, 6H), 7.80 (d, J = 8.0 Hz, 1H), 8.10-8.13 (m, 1H), 8.61 (d, J = 8.0 Hz, 1H), 9.18 (s, 1H). ^{13}C NMR (100 MHz, CF_3CO_2D): δ 173.2, 158.8, 158.7, 151.1, 150.0, 148.3, 147.4, 140.9, 136.5, 131.2, 131.1, 130.7, 130.6, 130.4, 123.8, 120.9, 120.9, 117.7, 117.4, 114.8, 114.7, 109.5, 102.3, 77.7, 55.2. *Anal*. Calcd for $C_{27}H_{17}N_5O_2S$: C 68.20, H 3.60, N 14.73. Found: C 68.29, H 3.64, N 14.76.

8-Cyano-6-(4-methoxyphenyl)-9-phenylamino-5*H*-thieno[3',2':2,3]pyrido[4,5-*d*]pyrido[1,2-*a*]pyrimidin-5-one (5d): Yellow crystals. mp > 300 ºC; IR (KBr): ν 3342 (NH), 2211 (CN), 1688 cm^{-1} (C=O). ^{1}H NMR (400 MHz, CF_3CO_2D): δ 4.15 (s, 3H), 7.28-7.31 (m, 2H), 7.61-7.74 (m, 8H), 7.89-7.91 (m, 1H), 8.18 (d, J = 8.6 Hz, 1H), 8.70 (d, J = 8.4 Hz, 1H), 9.27 (s, 1H). ^{13}C NMR (100 MHz, CF_3CO_2D): δ 173.2, 163.1, 159.8, 151.5, 150.1, 148.4, 147.4, 141.4, 136.7, 131.4, 130.7, 130.7, 130.5, 130.3, 123.5, 121.9, 121.2, 117.7, 114.7, 108.8, 101.9, 77.8, 55.1. *Anal*. Calcd for $C_{27}H_{17}N_5O_2S$: C 68.20, H 3.60, N 14.73. Found: C 68.27, H 3.63, N 14.75.

8-Cyano-6-(3,4-dimethoxyphenyl)-9-phenylamino-5*H*-thieno[3',2':2,3]pyrido[4,5-*d*]pyridolo[1,2-*a*]-pyrimidin-5-one (5e): Yellow crystals. mp > 300 ºC; IR (KBr): ν 3348 (NH), 2209 (CN), 1683 cm^{-1} (C=O). ^{1}H NMR (400 MHz, CF_3CO_2D): δ 4.05 (s, 3H), 4.15 (s, 3H), 7.31-7.33 (m, 2H), 7.36 (d, J = 8.4 Hz, 1H), 7.56-7.58 (m, 2H), 7.71-7.73 (m, 4H), 8.21 (d, J = 8.4 Hz, 1H), 7.91 (d, J = 8.2 Hz, 1H), 8.70 (d, J = 8.4 Hz, 1H), 9.30 (s, 1H). ^{13}C NMR (100 MHz, CF_3CO_2D): δ 173.1, 158.9, 152.4, 151.2, 149.9, 148.4, 148.3, 147.3, 141.1, 136.4, 131.2, 130.6, 130.3, 123.3, 122.9, 121.7, 120.9, 117.6, 116.0, 111.8, 111.3, 108.9, 102.0, 77.6, 55.4, 54.9. *Anal*. Calcd for $C_{28}H_{19}N_5O_3S$: C 66.52, H 3.79, N 13.85. Found: C 66.59, H 3.82, N 13.87.

8-Cyano-6-(4-hydroxyphenyl)-9-phenylamino-5*H*-thieno[3',2':2,3]pyrido[4,5-*d*]pyrido[1,2-*a*]pyrimidin-5-one (5f): Yellow crystals. mp > 300 ºC; IR (KBr): ν 3348 (NH), 3321 (OH), 2216 (CN), 1682 cm^{-1} (C=O). ^{1}H NMR (400 MHz, CF_3CO_2D): δ 7.26 (d, J = 8.8 Hz, 2H), 7.51 (d, J = 8.8 Hz, 2H), 7.60-7.67 (m, 6H), 7.83-7.87 (m, 1H), 7.85 (d, J = 8.6 Hz, 1H), 8.65-8.67 (m, 1H), 9.27 (s, 1H). ^{13}C NMR (100 MHz, CF_3CO_2D): δ 173.2, 159.6, 158.5, 151.3, 149.9, 148.6, 148.3, 147.3, 141.2, 136.5, 131.3, 130.7, 130.6, 130.4, 123.4, 122.2, 120.9, 117.6, 116.0, 108.9, 101.9, 77.6. *Anal*. Calcd for $C_{26}H_{15}N_5O_2S$: C 67.67, H 3.28, N 15.18. Found: C 67.74, H 3.30, N 15.21.

8-Cyano-6-(2-fluorophenyl)-9-phenylamino-5*H*-thieno[3',2':2,3]pyrido[4,5-*d*]pyridolo[1,2-*a*]pyrimidin-5-one (5g): Yellow crystals. mp > 300 ºC; IR (KBr): ν 3345 (NH), 2213 (CN), 1686 cm^{-1} (C=O). ^{1}H NMR (400 MHz, CF_3CO_2D): δ 7.30-7.33 (m, 2H), 7.49-7.61 (m, 8H), 7.66-7.69 (m, 1H), 8.09 (d, J = 8.4 Hz, 1H), 8.61-8.63 (m, 1H), 9.28 (s, 1H). ^{13}C NMR (100 MHz, CF_3CO_2D): δ 173.2, 158.3, 154.0, 151.0, 150.2, 148.9, 147.5, 140.9, 136.6, 135.4, 135.3, 131.4, 130.7, 130.6, 130.5, 129.2, 124.9, 123.5, 121.1, 117.8, 117.4, 109.4, 103.3, 77.9. *Anal*. Calcd for $C_{26}H_{14}FN_5OS$: C 67.38, H 3.04, N 15.11. Found: C 67.46, H 3.14, N 15.12.

8-Cyano-6-(4-fluorophenyl)-9-phenylamino-5*H*-thieno[3',2':2,3]pyrido[4,5-*d*]pyridolo[1,2-*a*]pyrimidin-5-one (5h): Yellow crystals. mp > 300 ºC; IR (KBr): *v* 3339 (NH), 2204 (CN), 1680 cm^{-1} (C=O). ^1H NMR (400 MHz, CF_3CO_2D): δ 7.29-7.32 (m, 2H), 7.44-7.48 (m, 2H), 7.59-7.61 (m, 6H), 7.77-7.80 (m, 1H), 8.08 (d, *J* = 8.6 Hz, 1H), 8.58-8.60 (m, 1H), 9.17 (s, 1H). ^{13}C NMR (100 MHz, CF_3CO_2D): δ 173.1, 158.8, 151.2, 149.9, 148.3, 147.3, 140.9, 136.4, 131.1, 130.6, 130.5, 130.4, 130.3, 124.8, 123.3, 120.9, 117.6, 116.4, 116.1, 109.4, 102.3, 77.6. *Anal*. Calcd for $C_{26}H_{14}FN_5OS$: C 67.38, H 3.04, N 15.11. Found: C 67.43, H 3.12, N 15.15.

6-(4-Chlorophenyl)-8-cyano-9-phenylamino-5*H*-thieno[3',2':2,3]pyrido[4,5-*d*]pyrido[1,2-*a*]pyrimidin-5-one (5i): Yellow crystals. mp > 300 ºC; IR (KBr): *v* 3345 (NH), 2218 (CN), 1686 cm^{-1} (C=O). ^1H NMR (400 MHz, CF_3CO_2D): δ 7.28-7.32 (m, 2H), 7.44-7.45 (m, 2H), 7.58-7.61 (m, 6H), 7.76-7.80 (m, 1H), 8.09 (d, *J* = 8.6 Hz, 1H), 8.57-8.60 (m, 1H), 9.18 (s, 1H). ^{13}C NMR (100 MHz, CF_3CO_2D): δ 172.8, 158.6, 151.4, 149.6, 148.2, 147.6, 141.2, 140.0, 136.3, 130.9, 130.7, 130.3, 129.4, 129.3, 129.2, 129.0, 127.2, 123.3, 120.7, 118.2, 102.3, 78.0. *Anal*. Calcd for $C_{26}H_{14}ClN_5OS$: C 65.07, H 2.94, N 14.59. Found: C 65.15, H 2.96, N 14.60.

8-Cyano-6-(4-nitrophenyl)-9-phenylamino-5*H*-thieno[3',2':2,3]pyrido[4,5-*d*]pyrido[1,2-*a*]pyrimidin-5-one (5j): Yellow crystals. mp > 300 ºC; IR (KBr): *v* 3363 (NH), 2212 (CN), 1689 cm^{-1} (C=O). ^1H NMR (400 MHz, CF_3CO_2D): δ 7.59-7.63 (m, 2H), 7.72-7.76 (m, 4H), 7.95-7.99 (m, 4H), 8.26-8.27 (m, 1H), 8.62-8.64 (m, 1H), 8.78-8.70 (m, 1H), 9.27 (s, 1H). ^{13}C NMR (100 MHz, CF_3CO_2D): δ 173.2, 156.7, 151.6, 150.4, 149.7, 148.9, 147.5, 140.8, 136.5, 135.9, 135.9, 131.2, 130.8, 130.6, 129.6, 124.1, 123.5, 121.3, 117.9, 110.5, 102.8, 78.1. *Anal*. Calcd for $C_{26}H_{14}N_6O_3S$: C 63.67, H 2.88, N 17.13. Found: C 63.75, H 2.90, N 17.15.

8-Cyano-6-(2-furyl)-9-phenylamino-5*H*-thieno[3',2':2,3]pyrido[4,5-*d*]pyrido[1,2-*a*]pyrimidin-5-one (5k): Yellow crystals. mp > 300 ºC; IR (KBr): *v* 3352 (NH), 2205 (CN), 1681 cm^{-1} (C=O). ^1H NMR (400 MHz, CF_3CO_2D): δ 7.06 (d, *J* = 4.8 Hz, 1H), 7.54-7.55 (m, 2H), 7.67-7.68 (m, 4H), 7.85-7.87 (m, 1H), 8.09-8.11 (m, 2H), 8.68-8.71 (m, 2H), 9.50 (s, 1H). ^{13}C NMR (100 MHz, CF_3CO_2D): δ 173.1, 151.3, 150.9, 149.8, 147.9, 146.9, 144.3, 141.6, 141.6, 136.4, 131.3, 130.6, 130.3, 129.4, 123.6, 123.3, 121.0, 117.3, 115.4, 106.7, 98.9, 77.6. *Anal*. Calcd for $C_{24}H_{13}N_6O_2S$: C 66.20, H 3.01, N 16.08. Found: C 66.27, H 3.04, N 16.11.

8-Cyano-6-(2-thienyl)-9-phenylamino-5*H*-thieno[3',2':2,3]pyrido[4,5-*d*]pyrido[1,2-*a*]pyrimidin-5-one (5l): Yellow crystals. mp > 300 ºC; IR (KBr): *v* 3348 (NH), 2214 (CN), 1684 cm^{-1} (C=O). ^1H NMR (400 MHz, CF_3CO_2D): δ 7.32-7.33 (m, 1H), 7.48-7.60 (m, 8H), 7.92-7.94 (m, 1H), 8.09-8.10 (m, 1H), 8.63-8.65 (m, 1H), 9.24 (s, 1H). ^{13}C NMR (100 MHz, CF_3CO_2D): δ 173.2, 153.3, 151.1, 150.1, 148.5, 147.3, 141.1, 136.6, 134.0, 133.9, 131.4, 130.7, 130.4, 130.3, 128.0, 127.7, 123.5, 121.1, 117.6, 109.4, 102.5, 77.7. *Anal*. Calcd for $C_{24}H_{13}N_5O_2S_2$: C 63.84, H 2.90, N 15.51. Found: C 63.92, H 2.93, N 15.54.

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