碘-二甲基亚砜促进新型四环噻唑并[3',2':2,3]吡啶并[4,5-*d*]吡啶并[1,2-*a*]嘧啶酮类衍生物的合成

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摘要 介绍了在碘-二甲基亚砜(I₂-DMSO)促进作用下, 通过 Pictet-Spengler 反应合成噻唑并[3',2':2,3]吡啶并[4,5-*d*]吡啶并[1,2-*a*]嘧啶酮(5)衍生物的合成方法. 该反应的关键中间体 2-(3-氨基-5-苯氨基噻唑-2-基)-4*H*-吡啶[1,2-*a*]嘧啶-4-酮(3), 由 2-氯甲基-4*H*-吡啶[1,2-*a*]嘧啶-4-酮(1)与 *N*-苯基-*N'*-氰基-咪唑硫代碳酸钾(2)通过 Thorpe-Ziegler 异构化反应制得. 该合成方法反应条件温和, 操作简单, 收率高.

关键词 吡啶[1,2-*a*]嘧啶; 噻唑并吡啶; Thorpe-Ziegler 异构化; Pictet-Spengler 反应; I₂-DMSO

Iodine-Dimethyl sulfoxide Promoted Synthesis of Novel Tetracyclic Thiazolo[3',2':2,3]pyrido[4,5-*d*]pyrido[1,2-*a*]pyrimidinones

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Abstract An iodine-dimethyl sulfoxide (I₂-DMSO) promoted efficient method is described for the synthesis of thiazolo[3',2':2,3]pyrido[4,5-*d*]pyrido[1,2-*a*]pyrimidin-5-ones (5) via Pictet-Spengler cyclization. The key intermediate, 2-(3-amino-5-phenylaminothiazolo-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) and potassium *N*-phenyl-*N'*-cyano-imido-thiocarbonate (2) by Thorpe-Ziegler isomerization. The novel synthetic method offers the advantage of mild reaction conditions, operational simplicity and higher yields.

Keywords pyrido[1,2-*a*]pyrimidine; thiazolopyridine; Thorpe-Ziegler isomerization; Pictet-Spengler reaction; I₂-DMSO

1 Introduction

Polyheterocycles are vital structural motifs with numerous applications in pharmaceutical and material science.^[1] Among them, pyrido[1,2-*a*]pyrimidines were classified as natural and non-natural products, which exhibited potential biological properties,^[2] such as tranquilizer,^[3] analgesics,^[4] antipsychotics,^[5] and anti-HIV agents.^[6] 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.^[7]

For example, this structural pattern is present in the known antiallergic agent ramastine^[8] and human leukocyte elastase inhibitor SSR69071.^[9] 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.^[10]

Molecular iodine is mild Lewis acid used in plethora of functional group transformations in organic synthesis as a catalyst in stoichiometric amount, and many reviews have

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Received April 12, 2019; revised May 26, 2019; published online June 12, 2019.

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documented its applications.^[11] Iodine has gained considerable attention as it is readily available, non-toxic cheap, easy to handle. It has become a preferred alternative for toxic and expensive acid catalysts. Because of numerous advantages associated with this ecofriendly element, iodine has been explored as a powerful catalyst for various organic transformations.^[12]

As part of our studies on construction of biologically important heterocycles,^[13] herein we report the synthesis of some new fused heterocyclic compounds thiazolo[3',2':2,3]pyrido[4,5-*d*]pyrido[1,2-*a*]pyrimidines by Pictet-Spengler reaction (Scheme 1).

5a R=Ph, **5b** R=4-MeC₆H₄, **5c** R=2-MeOC₆H₄, **5d** R=4-MeOC₆H₄, **5e** R=3,4-(MeO)₂C₆H₃, **5f** R=4-HOC₆H₄, **5g** R=2-FC₆H₄, **5h** R=4-FC₆H₄, **5i** R=4-ClC₆H₄, **5j** R=4-NO₂C₆H₄, **5k** R=2-furyl, **5l** R=2-thienyl

Scheme 1 Syntheses of thiazolopyrido-fused pyridopyrimidines

2 Results and discussion

To access the thiazolo[3',2':2,3]pyrido[4,5-*d*]pyrido[1,2-*a*]pyrimidin-5-ones, we envisioned a strategy by which the key reaction step of Pictet-Spengler cyclization consists of the condensation reaction of amine **3** with aromatic aldehydes. The key intermediate amine, 2-(3-amino-5-phenylaminothiazolo-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-phenylamino-ethen-1-yl)thiolate (**2**) via Thorpe-Ziegler isomerization^[14] in 85% yield. Elemental analysis (C₁₉H₁₃N₅OS) and spectral data supported its structure.

In an initial endeavor, benzaldehyde **4a** as model aromatic aldehyde to react with equimolar amounts of intermediate amine **3** for the preparation of 6-phenyl-9-phenylamino-5*H*-thiazolo[3',2':2,3]pyrido[4,5-*d*]pyrido[1,2-*a*]pyrimidin-5-one (**5a**) was selected and the optimal reaction conditions was investigated.

The reaction was conducted by using 10 mol% of I₂ as catalyst in dimethyl sulfoxide (DMSO) at 80 °C to give unexpected **5a** in 67% yield (Table 1, Entry 1). Increasing loading of I₂ catalyst to 20 mol% facilitated reaction rate and gave a higher yield (78%, Entry 2), whereas a visible drop in the yield was observed when the amount of I₂ was further increased to 30 mol% (Entry 3). The subsequent evaluation of reaction temperatures was conducted (Entries

2, 4 and 5). The reaction worked more effectively at 90 °C delivering the product **5a** in 86% yield (Entry 4). The yield leveled off when the temperature was further elevated to 100 °C (Entry 5). Afterward, other solvents, such as HOAc DMF and MeCN were utilized to investigate the solvent effect on the reaction outcomes in this cyclization (Entries 6~8), and it was found that all these solvents were inferior to DMSO in terms of reaction yields (Entry 4).

In addition, different catalysts such as sulfamic acid (SA), trifluoroacetic acid (TFA), and *p*-toluenesulfonic acid (*p*-TsOH) were screened for the optimal reaction conditions. The best catalytic activity was observed using I₂ in DMSO compared to other catalysts (Table 1, Entries 9~11).

Table 1 Optimization of reaction conditions on the synthesis of **5a**^a

Entry	Catalyst (mol%)	Solvent	Temp./°C	Time/h	Yield/%
1	I ₂ (10)	DMSO	80	11	67
2	I ₂ (20)	DMSO	80	9	78
3	I ₂ (30)	DMSO	80	8	76
4	I ₂ (20)	DMSO	90	9	86
5	I ₂ (20)	DMSO	100	8	82
6	I ₂ (20)	HOAc	90	8	73
7	I ₂ (20)	DMF	90	12	77
8	I ₂ (20)	MeCN	90	15	52
9	SA (20)	DMSO	90	10	70
10	TFA (20)	DMSO	90	8	74
11	<i>p</i> -TsOH (20)	DMSO	90	8	75

^a Reaction conditions: **3** (1.0 mmol), benzaldehyde (**4a**, 1.0 mmol), solvent (10 mL).

With these optimized reaction conditions, the versatility of the methodology for the preparation of thiazolopyridine-fused pyrido[1,2-*a*]pyrimidines was examined. The substrate scope of the I₂-DMSO catalyzed coupling of **1** with aromatic aldehydes **4** is shown in Table 2.

It was found that 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, it is concluded that the electronic nature of the substituents of aldehydes has no significant effect on this reaction.

When this methodology was applied to aliphatic aldehyde (such as butyraldehyde, **4m**) or ethyl glyoxylate (**4n**), no little product (**5m** or **4n**) was obtained after 24 h under the reaction conditions.

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-chloromethyl-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**1**) and potassium *N*-phenyl-*N'*-cyanoimido-thio-carbonate (**2**). Then, the ether **A** occurred via Thorpe-Ziegler isomerization reaction to generate 2-(3-amino-5-phenylaminothiazolo-2-yl)-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**3**). Next, the intermediate amine **3** underwent

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

Entry	R	4	Time/h	Product	Yield/%
1	C ₆ H ₅	4a	9	5a	86
2	4-MeC ₆ H ₄	4b	9	5b	87
3	2-MeOC ₆ H ₄	4c	11	5c	78
4	4-MeOC ₆ H ₄	4d	8	5d	88
5	3,4-(MeO) ₂ C ₆ H ₃	4e	8	5e	85
6	4-HOC ₆ H ₄	4f	8	5f	82
7	2-FC ₆ H ₄	4g	11	5g	79
8	4-FC ₆ H ₄	4h	10	5h	86
9	4-ClC ₆ H ₄	4i	11	5i	87
10	4-NO ₂ C ₆ H ₄	4j	12	5j	78
11	2-Furyl	4k	10	5k	75
12	2-Thienyl	4l	12	5l	82
13	<i>n</i> -Bu	4m	24	5m	0
14	CO ₂ Et	4n	24	5n	0

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

cationic π -cyclization with aldehyde (**4**) under Pictet-Spengler cyclization promoted by I₂ to form **C** which is further oxidized by DMSO to give tetracyclic product **5**.

3 Conclusions

Based on 6,6,6,5-tetracyclic systems, an efficient and versatile method for the preparation of thiazolopyridine-fused pyrido[1,2-*a*]pyrimidines was developed by using the modified Pictet-Spengler reaction promoted by molecular iodine in DMSO. This method has the advantages of readily available starting materials, mild reaction conditions and operational simplicity.

4 Experimental section

Melting points were determined in open capillaries and are uncorrected. The NMR spectra were recorded with a Bruker Avance 400 spectrometer (400 MHz for ¹H and 100 MHz for ¹³C) using TMS an internal reference. IR spectra were measured on Shimadzu FTIR-8300 spectro photometer. C, H and N analyses were performed by a HP-MOD 1106 microanalyzer. The preparation of 2-chloromethyl-4H-pyrido[1,2-*a*]pyrimidin-4-one (**1**)^[15] and potassium *N*-phenyl-*N'*-cyano-imido-thiocarbonate (**2**)^[16] were according to the literature procedure. All other chemicals used in this study were commercially available.

4.1 Synthesis of 2-(3-amino-5-phenylaminothiazolo-2-yl)-4H-pyrido[1,2-*a*]pyrimidin-4-one (**3**)

To a solution of 2-chloromethyl-4H-pyrido[1,2-*a*]pyrimidin-4-one (**1**) (1.94 g, 10.0 mmol) in DMF (25 mL) was added potassium *N*-phenyl-*N'*-cyanoimido-thiocarbonate (**2**) (2.15 g, 10.0 mmol), and anhydrous potassium carbonate (2.76 g, 20.0 mmol). The mixture was heated at 100 °C for 5 h (monitored by TLC). After cooling to room temperature, water (50 mL) was added and stirred for 20 min. The solid was filtered and recrystallized from HOAc to give **3** 2.84 g, yield 85%. Yellow crystals. m.p. > 300 °C; ¹H NMR (400 MHz, DMSO-*d*₆) δ : 5.67 (s, 1H), 7.03~7.06 (m, 1H), 7.11~7.14 (m, 1H), 7.34~7.38 (m, 2H), 7.58~7.70 (m, 5H), 7.84 (t, *J*=8.0 Hz, 1H), 8.82 (d, *J*=8.4 Hz, 1H), 10.63 (s, 1H); IR (KBr) $\nu_{\max}$: 3438, 3361 (N—H), 1680 (C=O) cm⁻¹. Anal. calcd for C₁₇H₁₃N₅O: C 60.88, H 3.91, N 20.88; found C 60.93, H 3.96, N 20.93.

4.2 General method for synthesis of 6-aryl-9-phenylamino-5H-thiazolo[3',2':2,3]pyrido[4,5-*d*]pyrido[1,2-*a*]pyrimidin-5-one derivatives (**5a**~**5l**)

To a stirred solution of 2-(3-amino-5-phenylaminothiazolo-2-yl)-4H-pyrido[1,2-*a*]pyrimidin-4-one (**3**) (335 mg, 1.0 mmol), aromatic aldehyde (1.0 mmol), and molecular iodine (50 mg, 0.2 mmol) in DMSO (10 mL) was heated at 90 °C (monitored by TLC). At the end of the reaction, the reaction mixture was cooled to room temperature, filtered and recrystallized from DMF to afford the corresponding products **5a**~**5l**.

Phenyl-9-phenylamino-5H-thiazolo[3',2':2,3]pyrido[4,5-*d*]pyrido[1,2-*a*]pyrimidin-5-one (**5a**): Yellow crystals. m.p. > 300 °C; ¹H NMR (400 MHz, CF₃CO₂D) δ : 7.28~7.31 (m, 2H), 7.43~7.56 (m, 8H), 7.76~7.79 (m, 1H), 7.93~7.97 (m, 1H), 8.10~8.13 (m, 1H), 8.53~8.57 (m, 1H), 9.15 (s, 1H); ¹³C NMR (100 MHz, CF₃CO₂D) δ : 171.8, 152.9, 151.4, 150.1, 149.8, 147.2, 146.9, 145.4, 135.4, 131.4, 131.1, 129.8, 128.8, 128.1, 127.9, 121.6, 120.8, 118.1, 117.4, 102.8; IR (KBr) $\nu_{\max}$: 3341 (N—H), 1682 (C=O) cm⁻¹. Anal. calcd for C₂₄H₁₅N₅O: C 68.39, H 3.59, N 16.62; found C 68.43, H 3.65, N 16.68.

6-(4-Methylphenyl)-9-phenylamino-5H-thiazolo[3',2':2,3]pyrido[4,5-*d*]pyrido[1,2-*a*]pyrimidin-5-one (**5b**): Yellow crystals. m.p. > 300 °C; ¹H NMR (400 MHz, CF₃CO₂D) δ : 2.57 (s, 3H), 7.53~7.54 (m, 6H), 7.64~7.69 (m,

4H), 7.85~7.89 (m, 1H), 8.16~8.18 (m, 1H), 8.65~8.69 (m, 1H), 9.26 (s, 1H); ^{13}C NMR (100 MHz, $\text{CF}_3\text{CO}_2\text{D}$) δ : 177.3, 159.2, 157.2, 151.2, 149.5, 146.9, 144.7, 141.3, 135.3, 130.9, 130.3, 129.8, 129.3, 127.8, 125.9, 122.9, 120.6, 117.3, 117.1, 101.2, 65.2; IR (KBr) ν_{max} : 3347 (N—H), 1683 (C=O) cm^{-1} . Anal. calcd for $\text{C}_{25}\text{H}_{17}\text{N}_5\text{OS}$: C 68.95, H 3.93, N 16.08; found C 68.98, H 3.97, N 16.13.

6-(2-Methoxyphenyl)-9-phenylamino-5*H*-thiazolo[3',2':2,3]pyrido[4,5-*d*]pyrido[1,2-*a*]pyrimidin-5-one (**5c**): Yellow crystals. m.p. > 300 °C; ^1H NMR (400 MHz, $\text{CF}_3\text{CO}_2\text{D}$) δ : 3.99 (s, 3H), 7.21~7.38 (m, 6H), 7.48~7.60 (m, 4H), 7.79~7.80 (m, 1H), 8.11~8.13 (m, 1H), 8.61~8.63 (m, 1H), 9.18 (s, 1H); ^{13}C NMR (100 MHz, $\text{CF}_3\text{CO}_2\text{D}$) δ : 177.2, 157.4, 156.8, 156.4, 150.7, 149.7, 147.1, 141.2, 135.5, 134.6, 134.5, 130.9, 130.4, 129.8, 128.9, 123.0, 121.0, 120.8, 118.2, 117.3, 111.2, 102.8, 54.6; IR (KBr) ν_{max} : 3343 (N—H), 1684 (C=O) cm^{-1} . Anal. calcd for $\text{C}_{25}\text{H}_{17}\text{N}_5\text{O}_2\text{S}$: C 66.50, H 3.80, N 15.51; found C 66.65, H 3.86, N 15.56.

6-(4-Methoxyphenyl)-9-phenylamino-5*H*-thiazolo[3',2':2,3]pyrido[4,5-*d*]pyrido[1,2-*a*]pyrimidin-5-one (**5d**): Yellow crystals. m.p. > 300 °C; ^1H NMR (400 MHz, $\text{CF}_3\text{CO}_2\text{D}$) δ : 3.90 (s, 3H), 7.08~7.11 (m, 2H), 7.38~7.98 (m, 8H), 7.69~7.71 (m, 1H), 7.88 (d, $J=8.6$ Hz, 1H), 8.52 (d, $J=8.6$ Hz, 1H), 9.13 (s, 1H); ^{13}C NMR (100 MHz, $\text{CF}_3\text{CO}_2\text{D}$) δ : 177.1, 162.8, 158.4, 157.1, 151.3, 149.5, 146.8, 141.3, 135.2, 130.9, 130.5, 130.4, 130.2, 129.7, 122.9, 121.6, 120.6, 117.0, 114.3, 101.0, 54.6; IR (KBr) ν_{max} : 3349 (N—H), 1691 (C=O) cm^{-1} . Anal. calcd for $\text{C}_{25}\text{H}_{17}\text{N}_5\text{O}_2\text{S}$: C 66.50, H 3.80, N 15.51; found C 66.54, H 3.83, N 15.53.

6-(3,4-Dimethoxyphenyl)-9-phenylamino-5*H*-thiazolo[3',2':2,3]pyrido[4,5-*d*]pyrido[1,2-*a*]pyrimidin-5-one (**5e**): Yellow crystals. m.p. > 300 °C; ^1H NMR (400 MHz, $\text{CF}_3\text{CO}_2\text{D}$) δ : 4.05 (s, 3H), 4.15 (s, 3H), 7.31~7.32 (m, 2H), 7.39~7.41 (m, 1H), 7.50~7.58 (m, 2H), 7.70~7.72 (m, 4H), 7.89~7.92 (m, 1H), 8.20~8.22 (m, 1H), 8.70~8.72 (m, 1H), 9.32 (s, 1H); ^{13}C NMR (100 MHz, $\text{CF}_3\text{CO}_2\text{D}$) δ : 177.3, 157.9, 157.2, 152.5, 151.4, 149.6, 148.2, 146.9, 141.6, 135.2, 131.0, 130.4, 129.9, 123.8, 123.1, 121.7, 120.7, 117.2, 111.8, 111.2, 109.3, 101.3, 55.2, 54.8; IR (KBr) ν_{max} : 3342 (N—H), 1685 (C=O) cm^{-1} . Anal. calcd for $\text{C}_{26}\text{H}_{19}\text{N}_5\text{O}_3\text{S}$: C 64.85, H 3.98, N 14.54; found C 64.89, H 4.04, N 14.59.

6-(4-Hydroxyphenyl)-9-phenylamino-5*H*-thiazolo[3',2':2,3]pyrido[4,5-*d*]pyrido[1,2-*a*]pyrimidin-5-one (**5f**): Yellow crystals. m.p. > 300 °C; ^1H NMR (400 MHz, $\text{CF}_3\text{CO}_2\text{D}$) δ : 7.24~7.27 (m, 2H), 7.50~7.52 (m, 2H), 7.60~7.67 (m, 6H), 7.83~7.87 (m, 1H), 8.14~8.17 (m, 1H), 8.65~8.67 (m, 1H), 9.27 (s, 1H); ^{13}C NMR (100 MHz, $\text{CF}_3\text{CO}_2\text{D}$) δ : 177.5, 159.0, 151.8, 149.9, 147.3, 144.2, 141.8, 136.9, 135.7, 131.4, 131.2, 130.7, 129.4, 125.4, 123.3, 122.5, 121.0, 117.6, 116.2, 101.6; IR (KBr) ν_{max} : 3353 (N—H), 3328 (OH), 1687 (C=O) cm^{-1} . Anal. calcd for $\text{C}_{24}\text{H}_{15}\text{N}_5\text{O}_2\text{S}$: C 65.89, H 3.46, N 16.01; found C 65.94, H 3.51, N 16.06.

6-(2-Fluorophenyl)-9-phenylamino-5*H*-thiazolo[3',2':2,

3]pyrido[4,5-*d*]pyrido[1,2-*a*]pyrimidin-5-one (**5g**): Yellow crystals. m.p. > 300 °C; ^1H NMR (400 MHz, $\text{CF}_3\text{CO}_2\text{D}$) δ : 7.43~7.63 (m, 10H), 7.73~7.84 (m, 1H), 8.25~8.28 (m, 1H), 8.76~8.79 (m, 1H), 9.37 (s, 1H); ^{13}C NMR (100 MHz, $\text{CF}_3\text{CO}_2\text{D}$) δ : 176.9, 158.5, 157.7, 153.5, 151.3, 150.0, 147.4, 141.2, 135.6, 135.2, 131.3, 130.6, 130.1, 129.3, 125.0, 123.3, 121.0, 118.3, 118.2, 117.6, 116.1, 103.2; IR (KBr) ν_{max} : 3342 (N—H), 1685 (C=O) cm^{-1} . Anal. calcd for $\text{C}_{24}\text{H}_{14}\text{FN}_5\text{OS}$: C 65.59, H 3.21, N 15.94; found C 65.64, H 3.27, N 15.97.

6-(4-Fluorophenyl)-9-phenylamino-5*H*-thiazolo[3',2':2,3]pyrido[4,5-*d*]pyrido[1,2-*a*]pyrimidin-5-one (**5h**): Yellow crystals. m.p. > 300 °C; ^1H NMR (400 MHz, $\text{CF}_3\text{CO}_2\text{D}$) δ : 7.28~7.32 (m, 2H), 7.44~7.48 (m, 2H), 7.59~7.61 (m, 6H), 7.77~7.80 (m, 1H), 8.08~8.11 (m, 1H), 8.58~8.60 (m, 1H), 9.18 (s, 1H); ^{13}C NMR (100 MHz, $\text{CF}_3\text{CO}_2\text{D}$) δ : 171.4, 158.9, 152.5, 151.1, 149.8, 149.4, 146.5, 144.9, 133.1, 131.1, 130.5, 129.4, 127.7, 124.4, 122.7, 121.3, 120.5, 117.6, 115.98, 102.5; IR (KBr) ν_{max} : 3346 (N—H), 1682 (C=O) cm^{-1} . Anal. calcd for $\text{C}_{24}\text{H}_{14}\text{FN}_5\text{OS}$: C 65.59, H 3.21, N 15.94; found C 65.66, H 3.25, N 15.98.

6-(4-Chlorophenyl)-9-phenylamino-5*H*-thiazolo[3',2':2,3]pyrido[4,5-*d*]pyrido[1,2-*a*]pyrimidin-5-one (**5i**): Yellow crystals. m.p. > 300 °C; ^1H NMR (400 MHz, $\text{CF}_3\text{CO}_2\text{D}$) δ : 7.22~7.34 (m, 10H), 7.53~7.55 (m, 1H), 7.82~7.84 (m, 1H), 8.36~8.41 (m, 1H), 8.95 (s, 1H); ^{13}C NMR (100 MHz, $\text{CF}_3\text{CO}_2\text{D}$) δ : 176.9, 157.7, 157.1, 151.2, 149.6, 146.9, 141.1, 139.6, 135.1, 130.8, 130.3, 129.8, 129.1, 128.9, 127.4, 122.9, 121.5, 120.6, 117.1, 101.6; IR (KBr) ν_{max} : 3358 (N—H), 1683 (C=O) cm^{-1} . Anal. calcd for $\text{C}_{24}\text{H}_{14}\text{ClN}_5\text{OS}$: C 63.23, H 3.10, N 15.36; found C 63.29, H 3.16, N 15.41.

6-(4-Nitrophenyl)-9-phenylamino-5*H*-thiazolo[3',2':2,3]pyrido[4,5-*d*]pyrido[1,2-*a*]pyrimidin-5-one (**5j**): Yellow crystals. m.p. > 300 °C; ^1H NMR (400 MHz, $\text{CF}_3\text{CO}_2\text{D}$) δ : 7.59~7.63 (m, 6H), 8.10~8.14 (m, 1H), 8.16~8.19 (m, 1H), 8.35~8.40 (m, 1H), 8.89 (s, 1H); ^{13}C NMR (100 MHz, $\text{CF}_3\text{CO}_2\text{D}$) δ : 171.8, 157.3, 153.4, 151.8, 150.1, 149.5, 149.4, 147.1, 145.1, 135.9, 133.4, 131.4, 131.1, 129.7, 129.5, 127.9, 123.8, 121.5, 116.3, 103.2; IR (KBr) ν_{max} : 3364 (N—H), 1687 (C=O) cm^{-1} . Anal. calcd for $\text{C}_{24}\text{H}_{14}\text{N}_6\text{O}_3\text{S}$: C 61.80, H 3.03, N 18.02; found C 61.85, H 3.07, N 18.05.

6-(2-Furyl)-9-phenylamino-5*H*-thiazolo[3',2':2,3]pyrido[4,5-*d*]pyrido[1,2-*a*]pyrimidin-5-one (**5k**): Yellow crystals. m.p. > 300 °C; ^1H NMR (400 MHz, $\text{CF}_3\text{CO}_2\text{D}$) δ : 7.05~7.06 (m, 1H), 7.54~7.68 (m, 6H), 7.81~7.83 (m, 1H), 8.09~8.10 (m, 2H), 8.68~8.71 (m, 2H), 9.51 (s, 1H); ^{13}C NMR (100 MHz, $\text{CF}_3\text{CO}_2\text{D}$) δ : 184.8, 177.8, 163.9, 154.2, 147.9, 146.4, 134.9, 133.7, 130.2, 129.9, 129.7, 129.3, 128.8, 128.3, 122.9, 121.6, 121.1, 120.3, 117.8, 103.3; IR (KBr) ν_{max} : 3345 (N—H), 1682 (C=O) cm^{-1} . Anal. calcd for $\text{C}_{22}\text{H}_{13}\text{N}_5\text{O}_2\text{S}$: C 64.22, H 3.18, N 17.02; found C 64.28, H 3.25, N 17.07.

6-(2-Thienyl)-9-phenylamino-5*H*-thiazolo[3',2':2,3]pyrido[4,5-*d*]pyrido[1,2-*a*]pyrimidin-5-one (**5l**): Yellow cry-

stals. m.p. > 300 °C; ^1H NMR (400 MHz, $\text{CF}_3\text{CO}_2\text{D}$) δ : 7.14~7.30 (m, 7H), 7.61~7.64 (m, 2H), 7.75~7.78 (m, 1H), 7.89~7.91 (m, 1H), 8.43~8.46 (m, 1H), 9.08 (s, 1H); ^{13}C NMR (100 MHz, $\text{CF}_3\text{CO}_2\text{D}$) δ : 177.1, 157.2, 152.4, 151.3, 149.6, 146.9, 141.4, 135.3, 135.2, 134.4, 134.4, 131.1, 130.4, 130.1, 128.5, 127.9, 123.1, 120.7, 117.2, 101.5; IR (KBr) ν_{max} : 3343 (N—H), 1684 (C=O) cm^{-1} . Anal. calcd for $\text{C}_{22}\text{H}_{13}\text{N}_5\text{OS}_2$: C 61.81, H 3.07, N 16.38; found C 61.85, H 3.12, N 16.40.

Supporting Information All Compounds NMR spectra were provided as supplementary data. The Supporting Information is available free of charge via the Internet at <http://sioc-journal.cn>.

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