Synthetic Communications®, 38: 1896–1908, 2008

ISSN: 0039-7911 print/1532-2432 online
DOI: 10.1080/00397910801997488

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Simple Procedure for the Synthesis of 5,7-Diarylpyrido[2,3-*d*]pyrimidine Derivatives catalyzed by KF-Alumina

Xiang-Shan Wang[1,2], Mei-Mei Zhang[2], Qing Li[1], Chang-Sheng Yao[1], and Shu-Jiang Tu[1,2]

[1]School of Chemistry and Chemical Engineering, Xuzhou Normal University, Xuzhou Jiangsu, China

[2]Key Laboratory of Biotechnology for Medical Plant, Xuzhou Normal University, Xuzhou Jiangsu, China

Abstract: A simple KF/Al_2O_3-catalyzed reaction of 1,3-diaryl-2-propen-1-one and 2,6-diamino-4-hydroxylpyrimidine in ethyl alcohol gave aromatized 5,7-diarylpyrido[2,3-*d*]pyrimidine derivative by air oxidation. On the other hand, the unaromatized intermediate products were isolated under dry nitrogen successfully. A possible reaction mechanism with two pathways to lose water was proposed based on the further experimental results; one of them was confirmed by ^1H NMR spectra of isolated intermediate product.

Keywords: Air oxidation; KF-Al_2O_3; pyrido[2,3-*d*]pyrimidine; Synthesis

INTRODUCTION

The utility of fluoride salts as potential bases in a variety of synthetic reactions has been recognized in recent years.[1] In particular, potassium fluoride coated with alumina (KF-alumina) has been a versatile solid-supported reagent developed by Ando et al. for alkylation.[2] Over the years, the reagent has found application in a large number of organic reactions. In our previous article,[3] we have reported the synthesis of pyrido[2,3-*d*]pyrimidine from aldehyde, malononitrile, or cyanoacetate with

Received October 12, 2007
Address correspondence to Xiang-Shan Wang, School of Chemistry and Chemical Engineering, Xuzhou Normal University, Xuzhou Jiangsu 221116, P. R. China. E-mail: xswang1974@yahoo.com

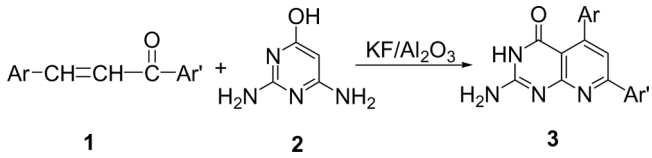
6-aminouracil successfully using this reagent. Pyrido[2,3-*d*]pyrimidines and their derivatives were reported to possess biological and pharmacological activities, such as antifolate activity,[4] antibacterial activity,[5] antimicrobial activity,[6] anti-inflammatory and analgesic activity,[7] antileishmanial activity,[8] anticonvulsant activity,[9] and anti-aggressive activity.[10] These prompted us to synthesize these compounds through another simple route. Herein we report a highly efficient method for synthesis of 5,7-diarylpyrido[2,3-*d*]pyrimidine derivatives by the reaction of 1,3-diaryl-2-propen-1-one and 2,6-diamino-4-hydroxylpyrimidine catalyzed by KF-Al_2O_3.

RESULTS AND DISCUSSION

When the 1,3-diaryl-2-propen-1-one (**1**) and 2,6-diamino-4-hydroxylpyrimidine (**2**) were treated with KF-Al_2O_3 in ethyl alcohol at 80 °C, the desired 5,7-diarylpyrido[2,3-*d*]pyrimidine derivatives (**3**) were obtained (Scheme 1) with high yields, which were the further aromatization products.

We began our study of the reaction shown in Scheme 1 by optimizing the reaction conditions for preparation of **3**. A summary of the optimization experiment is provided in Table 1. The results showed that at room temperature, no reaction took place (Table 1, Entry 1). The reaction was first carried out in EtOH in the absence of KF/Al_2O_3; only trace of **3a** was observed (Table 1, entry 3). Similar reactions were then attempted in the presence of KF/Al_2O_3 with 50, 100, and 150 mg. From Table 1 (entries 4, 5 and 6), we could see using of just 100 mg of KF-Al_2O_3 at 80 °C in EtOH was sufficient to push the reaction forward. Higher amounts of the catalyst did not improve the results to a greater extent. In addition, MeCN and DMF were also tested as the reaction solvents. In these cases, product **3a** was formed in slightly lower yield (Table 1, entries 7 and 8).

To demonstrate the efficiency and scope of the present method, a variety of 1,3-diaryl-2-propen-1-ones were subjected to reaction with 2,6-diamino-4-hydroxyl pyrimidine at the same reaction conditions. As



1 **2** **3**

Scheme 1. The reaction of 1,3-diaryl-2-propen-1-one and 2,6-diamino-4-hydroxylpyrimidine catalyzed KF-Al_2O_3.

Table 1. Yields of product **3a** at different reaction conditions[a]

Entry	Catalyst amount (mg)	Temp. (°C)	Solvent	Yields (%)[b]
1	100	0	EtOH	0
2	100	50	EtOH	72
3	0	80	EtOH	trace
4	50	80	EtOH	65
5	**100**	**80**	**EtOH**	**78**
6	150	80	EtOH	78
7	100	80	CH_3CN	74
8	100	90	DMF	76

[a]Reaction condition: 10 mL solvent, 2 mmol **1**, 2 mmol **2**.
[b]Isolated yields.

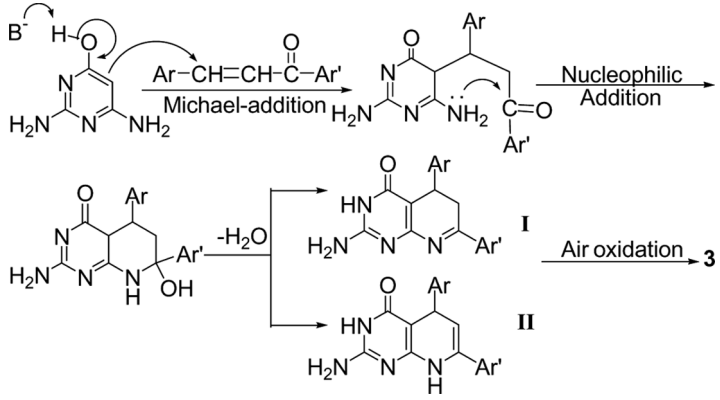
shown in Table 2, we can see the reactions proceeded smoothly to afford the corresponding products **3** in good yields. All the products were characterized by ^{1}H NMR, IR spectra, and elemental analysis.

According to the structure of **3**, a sequential reaction of the Michael addition reaction, intramolecular nucleophilic addition, and aromatization may take place during the formation of the product (Scheme 2).

Table 2. KF/Al_2O_3-catalyzed reactions of 1,3-diaryl-2-propen-1-ones and 2,6-diamino-4-hydroxylpyrimidine[a]

Entry	Ar	Ar′	Products	Time (h)	Yields (%)[b]
1	C_6H_5	4-$CH_3OC_6H_4$	**3a**	10	79
2	2-Thiophenyl	C_6H_5	**3b**	9	81
3	3-ClC_6H_4	4-ClC_6H_4	**3c**	8	86
4	C_6H_5	4-ClC_6H_4	**3d**	8	81
5	4-ClC_6H_4	4-ClC_6H_4	**3e**	10	80
6	3-$CH_3C_6H_4$	C_6H_5	**3f**	12	79
7	C_6H_5	4-FC_6H_4	**3g**	9	84
8	2-ClC_6H_4	4-ClC_6H_4	**3h**	9	85
9	C_6H_5	2-ClC_6H_4	**3i**	9	82
10	3-$NO_2C_6H_4$	C_6H_5	**3j**	8	83
11	4-ClC_6H_4	4-BrC_6H_4	**3k**	8	84
12	4-$CH_3OC_6H_4$	C_6H_5	**3l**	10	80

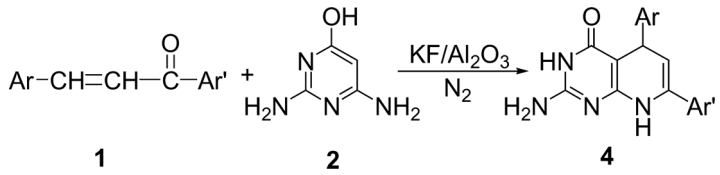
[a]Reaction condition: 10 mL EtOH, 2 mmol **1**, 2 mmol **2**, 100 mg KF-Al_2O_3, 80°C.
[b]Isolated yields.



Scheme 2. The possible reaction mechanism.

From Scheme 2, two possible pathways were proposed to lose the water, giving the two unaromatized intermediate products **I** or **II**. It was reported[11] that the dihydropyrido[2,3-*d*]pyrimidine derivatives were unstable to their corresponding aromatization products by air oxidation automatically. To prevent the air oxidation and obtain the unaromatized intermediates, we tested the same reaction under dry nitrogen (Scheme 3). To our delight, the desired intermediate **II** was isolated, which was confirmed by ^{1}H NMR spectra. The spectrum of **4a** was shown in Fig. 1. Obviously, it was typical AM system for protons on the positions of 5 and 6, not ABX system, so the structure of the intermediate was **II** rather than **I**. The results of unaromatized 5,7-diarylpyrido[2,3-*d*]pyrimidine derivatives are summarized in Table 3.

If the unaromatized intermediate product **4f** was treated in EtOH at 80 °C for 10 h (Scheme 4), it gave the corresponding **3f** in 72% yield. This result indicated that the air oxidation took place in the formation of products **3**.



Scheme 3. The reaction of 1,3-diaryl-2-propen-1-one and 2,6-diamino-4-hydroxylpyrimidine under N_2.

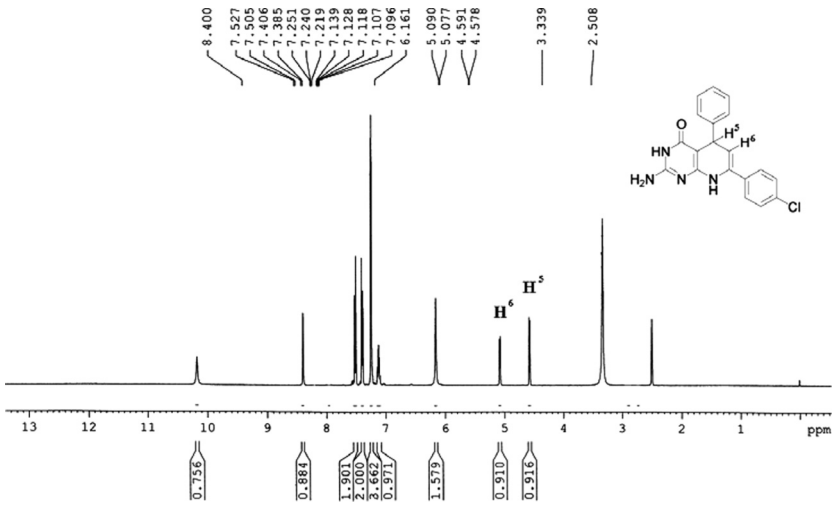


Figure 1. ^{1}H NMR of compound **4a** (400 MHz).

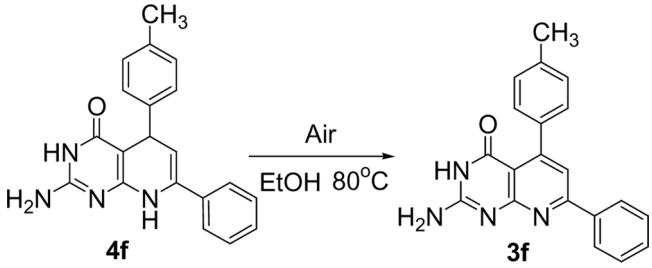
CONCLUSION

In conclusion, we found a convenient method for the synthesis of 5,7-diarylpyrido[2,3-*d*]pyrimidine derivatives by the reaction of 1,3-diaryl-2-propen-1-one and 2,6-diamino-4-hydroxylpyrimidine catalyzed by KF-Al_2O_3. This method has the advantage of an easy workup, milder

Table 3. KF-Al_2O_3-catalyzed reactions of 1,3-diaryl-2-propen-1-one and 2,6-diamino-4-hydroxylpyrimidine under nitrogen[a]

Entry	Ar	Ar′	Products	Time (min)	Yields (%)[b]
1	C_6H_5	4-ClC_6H_4	**4a**	**40**	**82**
2	3,4-$(CH_3O)_2C_6H_3$	C_6H_5	**4b**	**45**	**81**
3	2-Thiophenyl	4-ClC_6H_4	**4c**	**50**	**83**
4	3-$NO_2C_6H_4$	C_6H_5	**4d**	**40**	**86**
5	3-$NO_2C_6H_4$	4-ClC_6H_4	**4e**	**60**	**80**
6	4-$CH_3C_6H_4$	C_6H_5	**4f**	**50**	**73**
7	C_6H_5	C_6H_5	**4g**	**60**	**82**
8	4-ClC_6H_4	C_6H_5	**4h**	**40**	**88**
9	4-$CH_3OC_6H_4$	C_6H_5	**4i**	**50**	**72**

[a]Reaction condition: 10 mL EtOH, 2 mmol **1**, 2 mmol **2**, 100 mg KF-Al_2O_3, 80 °C.
[b]Isolated yields.



Scheme 4. The subsequent aromatization in air.

reaction conditions, and good yields in the synthesis of these potential active compounds.

EXPERIMENTAL

Melting points were determined in open capillaries and are uncorrected. IR spectra were recorded on a Tensor 27 spectrometer in KBr. ^{1}H NMR spectra were obtained for solution in DMSO-d_6 with Me_4Si as internal standard using an Inova-400 spectrometer. Elemental analyses were carried out using a Perkin-Elmer 2400 II analyzer.

The 2,6-diamino-4-hydroxylpyrimidine was purchased from Aldrich Chemical Company, Inc. The starting materials of 1,3-diaryl-2-propen-1-one were prepared as references reported.[12]

General Procedure for the 2-Amino-5,7-diarylpyrido[2,3-*d*] pyrimidine-4(3H)-one 3

A dry 100-mL flask was charged with 1,3-diaryl-2-propen-1-one **1** (2 mmol), 2,6-diamino-4-hydroxylpyrimidine **2** (2 mmol), KF/Al_2O_3 (100 mg), and EtOH (10 mL). The mixture was stirred at 80 °C for 8–12 h. Then after being cooled to room temperature, the solid material was filtered off. The crude product was purified by recrystallization from DMF and water, followed by keeping at 80°C for 2 h in a vacuum to give **3**.

Data

2-Amino-7-(4-methoxylphenyl)-5-phenylpyrido[2,3-*d*] pyrimidine-4(3*H*)-one **3a**

This compound was obtained as yellow powder, mp >300 °C; IR (KBr): ν_{max} 3329, 3154, 2929, 1647, 1610, 1509, 1455, 1301, 1249, 1207, 1123,

1108, 1032, 852, 832, 799, 766, 745; ^{1}H NMR (DMSO-d_6): δ 3.81 (s, 3H, CH_3O), 6.69 (b, 2H, NH_2), 7.04 (d, $J = 8.8$ Hz, 2H, ArH), 7.32 (s, 1H, ArH), 7.38 (s, 5H, ArH), 8.16 (d, $J = 8.8$ Hz, 2H, ArH), 10.91 (b, 1H, ArH). Anal. calcd. for $C_{20}H_{16}N_4O_2$: C, 69.76; H, 4.68; N, 16.27. Found: C, 69.87; H, 4.50; N, 16.33.

2-Amino-7-phenyl-5-thiophenylpyrido[2,3-*d*]pyrimidine-4(3*H*)-one **3b**

This compound was obtained as yellow powder, mp >300 °C; IR (KBr): ν_{max} 3305, 3255, 3144, 3071, 2835, 1696, 1672, 1659, 1578, 1547, 1441, 1409, 1329, 1287, 1253, 1218, 1102, 889, 851, 777, 690; ^{1}H NMR (DMSO-d_6): δ 6.72 (b, 2H, NH_2), 7.17–7.13 (m, 1H, ArH), 7.35–7.51 (m, 6H, ArH), 7.69 (d, $J = 4.8$ Hz, 1H, ArH), 8.16–8.18 (m, 2H, ArH), 11.08 (b, 1H, NH). Anal. calcd. for $C_{17}H_{12}N_4OS$: C, 63.73; H, 3.78; N, 17.49. Found: C, 63.90; H, 3.68; N, 17.55.

2-Amino-7-(4-chlorophenyl)-5-(3-chlorophenyl)pyrido[2,3-*d*] pyrimidine-4(3*H*)-one **3c**

This compound was obtained as yellow powder, mp >300 °C; IR (KBr): ν_{max} 3088(b), 1680, 1573, 1549, 1475, 1408, 1357, 1284, 1233, 1162, 1121, 1091, 1011, 974, 877, 834, 820, 789, 710, 696; ^{1}H NMR (DMSO-d_6): δ 6.74 (b, 2H, NH_2), 7.34–7.47 (m, 5H, ArH), 7.56 (d, $J = 8.4$ Hz, 2H, ArH), 8.24 (d, $J = 8.8$ Hz, 2H, ArH), 11.02 (b, 1H, NH). Anal. calcd. for $C_{19}H_{12}Cl_2N_4O$: C, 59.55; H, 3.16; N, 14.62. Found: C, 59.68; H, 3.09; N, 14.78.

2-Amino-7-(4-chlorophenyl)-5-phenylpyrido[2,3-*d*] pyrimidine-4(3*H*)-one **3d**

This compound was obtained as yellow powder, mp >300 °C; IR (KBr): ν_{max} 3468, 3306, 3221, 3067, 1663, 1597, 1549, 1524, 1458, 1385, 1254, 1239, 1181, 1092, 1043, 1012, 858, 833, 825, 788, 760, 742, 696; ^{1}H NMR (DMSO-d_6): δ 6.72 (b, 2H, NH_2), 7.42 (s, 5H, ArH), 7.56 (s, 1H, ArH), 7.34–7.47 (m, 5H, ArH), 7.60 (d, $J = 8.4$ Hz, 2H, ArH), 8.24 (d, $J = 8.4$ Hz, 2H, ArH), 10.98 (b, 1H, NH). Anal. calcd. for $C_{19}H_{13}ClN_4O$: C, 65.43; H, 3.76; N, 16.06. Found: C, 65.50; H, 3.59; N, 16.13.

2-Amino-5,7-di(4-chlorophenyl)pyrido[2,3-*d*]pyrimidine-4(3*H*)-one **3e**

This compound was obtained as yellow powder, mp >300 °C; IR (KBr): ν_{max} 3315, 3158, 1641, 1575, 1520, 1487, 1455, 1414, 1393, 1357, 1274,

1091, 1013, 831; ^{1}H NMR (DMSO-d_6): δ 6.73 (b, 2H, NH_2), 7.41–7.46 (m, 5H, ArH), 7.56 (d, $J = 8.4$ Hz, 2H, ArH), 8.23 (d, $J = 8.4$ Hz, 2H, ArH), 11.00 (b, 1H, NH). Anal. calcd. for $C_{19}H_{12}Cl_2N_4O$: C, 59.55; H, 3.16; N, 14.62. Found: C, 59.76; H, 3.10; N, 14.71.

2-Amino-5-(4-methylphenyl)-7-phenylpyrido[2,3-*d*] pyrimidine-4(3*H*)-one **3f**

This compound was obtained as yellow powder, mp >300 °C; IR (KBr): ν_{max} 3149(b), 3031, 2918, 2856, 1683, 1654, 1625, 1575, 1541, 1524, 1413, 1361, 1280, 1253, 1156, 1115, 812; ^{1}H NMR (DMSO-d_6): δ 2.38 (s, 3H, CH_3), 6.68 (b, 2H, NH_2), 7.20 (d, $J = 8.0$ Hz, 2H, ArH), 7.30 (d, $J = 8.0$ Hz, 2H, ArH), 7.35 (s, 1H, ArH), 7.49–7.51 (m, 3H, ArH), 8.16–8.18 (m, 2H, ArH), 10.93 (b, 1H, NH). Anal. calcd. for $C_{20}H_{16}N_4O$: C, 73.15; H, 4.91; N, 17.06. Found: C, 73.28; H, 4.77; N, 17.25.

2-Amino-7-(4-fluorophenyl)-5-phenylpyrido[2,3-*d*] pyrimidine-4(3*H*)-one **3g**

This compound was obtained as yellow powder, mp >300 °C; IR (KBr): ν_{max} 3315, 3141, 3081, 1692, 1673, 1657, 1605, 1575, 1547, 1512, 1492, 1415, 1357, 1285, 1234, 1157, 985, 845, 772, 691; ^{1}H NMR (DMSO-d_6): δ 6.70 (b, 2H, NH_2), 7.30–7.39 (m, 8H, ArH), 8.24–8.32 (m, 2H, ArH), 10.94 (b, 1H, NH). Anal. calcd. for $C_{19}H_{13}FN_4O$: C, 68.67; H, 3.94; N, 16.86. Found: C, 68.55; H, 3.89; N, 16.70.

2-Amino-7-(4-chlorophenyl)-5-(2-chlorophenyl)pyrido[2,3-*d*] pyrimidine-4(3*H*)-one **3h**

This compound was obtained as yellow powder, mp >300 °C; IR (KBr): ν_{max} 3305(b), 3066, 1645, 1592, 1573, 1547, 1518, 1477, 1412, 1361, 1306, 1254, 1092, 1056, 1032, 1012, 834, 825, 744; ^{1}H NMR (DMSO-d_6): δ 6.24 (b, 2H, NH_2), 7.32–7.50 (m, 5H, ArH), 7.56 (d, $J = 8.4$ Hz, 2H, ArH), 8.23 (d, $J = 8.4$ Hz, 2H, ArH), 10.99 (b, 1H, NH). Anal. calcd. for $C_{19}H_{12}Cl_2N_4O$: C, 59.55; H, 3.16; N, 14.62. Found: C, 59.58; H, 3.23; N, 14.69.

2-Amino-7-(2-chlorophenyl)-5-phenylpyrido[2,3-*d*] pyrimidine-4(3*H*)-one **3i**

This compound was obtained as yellow powder, mp >300 °C;IR (KBr): ν_{max} 3320, 3255, 3156, 1693, 1673, 1607, 1569, 1547, 1492, 1479, 1410, 1344, 1251, 1235, 1162, 881, 796, 778, 699; ^{1}H NMR (DMSO-d_6): δ 6.70

(b, 2H, NH_2), 7.40 (s, 5H, ArH), 7.45 (s, 1H, ArH), 7.51–7.55 (m, 2H, ArH), 8.16 (d, $J = 7.2$ Hz, 1H, ArH), 8.26 (d, $J = 1.6$ Hz, 1H, ArH), 10.97 (b, 1H, NH). Anal. calcd. for $C_{19}H_{13}ClN_4O$: C, 65.43; H, 3.76; N, 16.06. Found: C, 65.55; H, 3.60; N, 16.23.

2-Amino-5-(3-nitrophenyl)-7-phenylpyrido[2,3-*d*] pyrimidine-4(3*H*)-one **3j**

This compound was obtained as yellow powder, mp >300 °C; IR (KBr): ν_{max} 3393, 3161(b), 1678, 1650, 1607, 1581, 1547, 1527, 1434, 1404, 1347, 1310, 1243, 1173, 1098, 778, 740, 697, 688; ^{1}H NMR (DMSO-d_6): δ 6.75 (b, 2H, NH_2), 7.51 (s, 4H, ArH), 7.68–7.72 (m, 1H, ArH), 7.89 (d, $J = 8.4$ Hz, 1H, ArH), 8.21–8.28 (m, 4H, ArH), 11.03 (b, 1H, NH). Anal. calcd. for $C_{19}H_{13}N_5O_3$: C, 63.51; H, 3.65; N, 19.49. Found: C, 63.66; H, 3.59; N, 19.28.

2-Amino-7-(4-bromophenyl)-5-(4-chlorophenyl)pyrido[2,3-*d*] pyrimidine-4(3*H*)-one **3k**

This compound was obtained as yellow powder, mp >300 °C; IR (KBr): ν_{max} 3294, 3120, 1682, 1624, 1595, 1572, 1541, 1520, 1485, 1411, 1358, 1276, 1255, 1093, 1072, 1011, 959, 856, 838, 815, 758; ^{1}H NMR (DMSO-d_6): δ 6.60 (b, 2H, NH_2), 7.36 (d, $J = 8.0$ Hz, 2H, ArH), 7.42 (s, 1H, ArH), 7.56–7.60 (m, 4H, ArH), 8.22 (d, $J = 8.4$ Hz, 2H, ArH), 11.02 (b, 1H, NH). Anal. calcd. for $C_{19}H_{12}BrClN_4O$: C, 53.36; H, 2.83; N, 13.10. Found: C, 53.30; H, 2.69; N, 13.13.

2-Amino-5-(4-methoxylphenyl)-7-phenylpyrido[2,3-*d*] pyrimidine-4(3*H*)-one **3l**

This compound was obtained as yellow powder, mp >300 °C; IR (KBr): ν_{max} 3288, 3113, 1683, 1653, 1625, 1608, 1578, 1541, 1511, 1456, 1419, 1403, 1362, 1279, 1248, 1178, 1161, 1114, 1033, 861, 830, 775; ^{1}H NMR (DMSO-d_6): δ 3.81 (s, 3H, CH_3O), 6.66 (s, 2H, NH_2), 6.95 (d, $J = 8.8$ Hz, 2H, ArH), 7.37 (d, $J = 8.8$ Hz, 2H, ArH), 7.47–7.54 (m, 3H, ArH), 8.17–8.19 (m, 2H, ArH), 10.95 (b, 1H, NH). Anal. calcd. for $C_{20}H_{16}N_4O_2$: C, 69.76; H, 4.68; N, 16.27. Found: C, 69.92; H, 4.54; N, 16.20.

General Procedure for the 2-Amino-5,7-diaryl-5,8-dihydropyrido [2,3-*d*]pyrimidine-4(3H)-one 4

A dry 100-mL flask was charged with 1,3-diaryl- 2-propen-1-one **1** (2 mmol), 2,6-diamino-4-hydroxylpyrimidine **2** (2 mmol), KF/Al_2O_3

(100 mg), and EtOH (10 mL) under dry nitrogen, The mixture was stirred at 80 °C for 40–60 min. Then after being cooled to room temperature, the solid material was filtered off and the crude product was purified by recrystallization from 95% EtOH to give **4**.

Data

2-Amino-7-(4-chlorophenyl)-5-phenyl-5,8-dihydropyrido[2,3-*d*] pyrimidine-4(3*H*)-one **4a**

This compound was obtained as yellow powder, mp 230–232 °C; IR (KBr): ν_{max} 3330, 2927, 1639, 1527, 1465, 1406, 1371, 1256, 1236, 1203, 1179, 1159, 1071, 1043, 1024, 1010, 822, 769, 700; ^{1}H NMR (DMSO-d_6): δ 4.58 (d, $J = 5.2$ Hz, 1H, CH), 5.09 (d, $J = 5.2$ Hz, 1H, CH=), 6.16 (b, 2H, NH_2), 7.10–7.14 (m, 1H, ArH), 7.22–7.25 (m, 4H, ArH), 7.40 (d, $J = 8.4$ Hz, 2H, ArH), 7.52 (d, $J = 8.4$ Hz, 2H, ArH), 8.40 (b, 1H, NH), 10.18 (b, 1H, NH). Anal. calcd. for $C_{19}H_{15}ClN_4O$: C, 65.05; H, 4.31; N, 15.97. Found: C, 64.90; H, 4.51; N, 15.89.

2-Amino-5-(3,4-dimethoxylphenyl)-7-phenyl-5,8-dihydropyrido [2,3-*d*]pyrimidine-4(3*H*)-one **4b**

This compound was obtained as yellow powder, mp 235–236 °C; IR (KBr): ν_{max} 3566, 3356, 3141, 1716, 1653, 1558, 1541, 1517,1457, 1418, 1316, 1259, 1180, 1138, 1026, 793, 735, 700; ^{1}H NMR (DMSO-d_6): δ 3.69 (s, 3H, CH_3O), 3.70 (s, 3H, CH_3O), 4.52 (d, $J = 5.2$ Hz, 1H, CH), 5.08 (d, $J = 5.2$ Hz, 1H, CH=), 6.14 (b, 2H, NH_2), 6.74 (d, $J = 8.4$ Hz, 1H, ArH), 6.84 (d, $J = 8.4$ Hz, 1H, ArH), 6.91 (s, 1H, ArH), 7.31–7.37 (m, 3H, ArH), 7.49–7.51 (m, 2H, ArH), 8.28 (b, 1H, NH), 10.16 (b, 1H, NH). Anal. calcd. for $C_{21}H_{20}N_4O_3$: C, 67.01; H, 5.36; N, 14.88. Found: C, 66.87; H, 5.54; N, 14.80.

2-Amino-7-(4-chlorophenyl)-5-(2-thiophenyl)-5,8-dihydropyrido [2,3-*d*]pyrimidine-4(3*H*)-one **4c**

This compound was obtained as yellow powder, mp 253–255 °C; IR (KBr): ν_{max} 3629, 3474, 3224, 3085, 2929, 1665, 1602, 1482, 1385, 1319, 1257, 1231, 1219, 1186, 1172, 1126, 1105, 1092, 1046, 1013, 860, 849, 827, 792, 772, 695, 669; ^{1}H NMR (DMSO-d_6): δ 4.88 (d, $J = 5.2$ Hz, 1H, CH), 5.17 (dd, $J = 5.2$ Hz, $J' = 1.6$ Hz, 1H, CH=), 6.20 (b, 2H, NH_2), 6.87–6.90 (m, 2H, ArH), 7.23 (dd, $J = 4.8$ Hz, $J' = 1.2$ Hz,

1H, ArH), 7.43 (d, $J = 8.8$ Hz, 2H, ArH), 7.54 (d, $J = 8.8$ Hz, 2H, ArH), 8.56 (b, 1H, NH), 10.25 (b, 1H, NH). Anal. calcd. for $C_{17}H_{13}ClN_4OS$: C, 57.22; H, 3.67; N, 15.70. Found: C, 57.10; H, 3.68; N, 15.92.

2-Amino-5-(3-nitrophenyl)-7-phenyl-5,8-dihydropyrido[2,3-*d*] pyrimidine-4(3*H*)-one **4d**

This compound was obtained as yellow powder, mp >300 °C; IR (KBr): ν_{max} 3327, 2927, 2729, 1645, 1526, 1466, 1406, 1349, 1257, 1236, 1209, 1187, 1161, 1096, 1044, 942, 918, 896, 852, 807, 772, 738, 701; ^{1}H NMR (DMSO-d_6): δ 4.78 (d, $J = 5.2$ Hz, 1H, CH), 5.08 (d, $J = 5.2$ Hz, 1H, CH=), 6.26 (b, 2H, NH_2), 7.34–7.38 (m, 3H, ArH), 7.51–7.53 (m, 2H, ArH), 7.56–7.60 (m, 1H, ArH), 7.75 (d, $J = 7.2$ Hz, 1H, ArH), 8.03 (dd, $J = 8.4$ Hz, $J' = 1.2$ Hz, 1H, ArH), 8.07 (s, 1H, ArH), 8.54 (b, 1H, NH), 10.24 (b, 1H, NH). Anal. calcd. for $C_{19}H_{15}N_5O_3$: C, 63.15; H, 4.18; N, 19.38. Found: C, 63.27; H, 4.22; N, 19.10.

2-Amino-7-(4-chlorophenyl)-5-(3-nitrophenyl)-5,8-dihydropyrido [2,3-*d*]pyrimidine-4(3*H*)-one **4e**

This compound was obtained as yellow powder, mp >300 °C; IR (KBr): ν_{max} 3216, 2927, 1653, 1599, 1525, 1471, 1412, 1389, 1348, 1256, 1180, 1094, 1049, 1013, 840, 806, 740, 678. ^{1}H NMR (DMSO-d_6): δ 4.77 (d, $J = 5.2$ Hz, 1H, CH), 5.11 (d, $J = 5.2$ Hz, 1H, CH=), 6.26 (b, 2H, NH_2), 7.42 (d, $J = 8.4$ Hz, 2H, ArH), 7.53 (d, $J = 8.4$ Hz, 2H, ArH), 7.55–7.60 (m, 1H, ArH), 7.74 (d, $J = 7.6$ Hz, 1H, ArH), 8.01–8.06 (m, 2H, ArH), 8.63 (b, 1H, NH), 10.27 (b, 1H, NH). Anal. calcd. for $C_{19}H_{14}ClN_5O_3$: C, 57.66; H, 3.57; N, 17.69. Found: C, 57.60; H, 3.68; N, 17.54.

2-Amino-5-(4-methylphenyl)-7-phenyl-5,8-dihydropyrido[2,3-*d*] pyrimidine-4(3*H*)-one **4f**

This compound was obtained as yellow powder, mp 223–224°C; IR (KBr): ν_{max} 3451, 3386, 3269, 3059, 2922, 1638, 1536, 1462, 1372, 1257, 1233, 1178, 1091, 1043, 1025, 813, 794, 776, 766, 699; ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 2.22 (s, 3H, CH_3), 4.52 (d, $J = 5.2$ Hz, 1H, CH), 5.06 (d, $J = 5.2$ Hz, 1H, CH=), 6.18 (b, 2H, NH_2), 7.03 (d, $J = 8.0$ Hz, 2H, ArH), 7.12 (d, $J = 8.0$ Hz, 2H, ArH), 7.30–7.35 (m, 3H, ArH), 7.47–7.50 (m, 2H, ArH), 8.29 (b, 1H, NH), 10.19 (b, 1H, NH). Anal. calcd. for $C_{20}H_{18}N_4O$: C, 72.71; H, 5.49; N, 16.96. Found: C, 72.65; H, 5.58; N, 16.87.

2-Amino-5,7-diphenyl-5,8-dihydropyrido[2,3-*d*]pyrimidine-4(3*H*)-one **4g**

This compound was obtained as yellow powder, mp 243–245 °C; IR (KBr): ν_{max} 3468, 3376, 3278, 3063, 2877, 1639, 1596, 1529, 1491, 1465, 1396, 1370, 1259, 1235, 1202, 1180, 1158, 1135, 1094, 1064, 1030, 877, 798, 771, 756, 699; ^{1}H NMR (DMSO-d_6): δ 4.58 (d, $J = 5.2$ Hz, 1H, CH), 5.06 (d, $J = 5.2$ Hz, 1H, CH=), 6.21 (b, 2H, NH_2), 7.10–7.13 (m, 1H, ArH), 7.24–7.39 (m, 6H, ArH), 7.48–7.50 (m, 3H, ArH), 8.34 (b, 1H, NH), 10.24 (b, 1H, NH). Anal. calcd. for $C_{19}H_{16}N_4O$: C, 72.13; H, 5.10; N, 17.71. Found: C, 72.28; H, 5.40; N, 17.62.

2-Amino-5-(4-chlorophenyl)-7-phenyl-5,8-dihydropyrido[2,3-*d*] pyrimidine-4(3*H*)-one **4h**

This compound was obtained as yellow powder, mp 228–230°C; IR (KBr): ν_{max} 3325, 2927, 1640, 1524, 1488, 1461, 1410, 1372, 1283, 1256, 1204, 1179, 1159, 1089, 1015, 936, 828, 795, 770, 699; ^{1}H NMR (DMSO-d_6): δ 4.60 (d, $J = 5.2$ Hz, 1H, CH), 5.04 (dd, $J = 5.2$ Hz, $J' = 1.6$ Hz, 1H, CH=), 6.19 (b, 2H, NH_2), 7.25–7.37 (m, 7H, ArH), 7.49 (d, $J = 8.0$ Hz, 2H, ArH), 8.38 (b, 1H, NH), 10.21 (b, 1H, NH). Anal. calcd. for $C_{19}H_{15}ClN_4O$: C, 65.05; H, 4.31; N, 15.97. Found: C, 64.88; H, 4.30; N, 16.09.

2-Amino-5-(4-methoxylphenyl)-7-phenyl-5,8-dihydropyrido[2,3-*d*] pyrimidine-4(3*H*)-one **4i**

This compound was obtained as yellow powder, mp 185–186 °C; IR (KBr): ν_{max} 3329, 3154, 2929, 2834, 1648, 1509, 1456, 1301, 1250, 1207, 1174, 1108, 1032, 852, 832, 799, 767, 746, 696; ^{1}H NMR (DMSO-d_6): δ 3.69 (s, 3H, CH_3O), 4.53 (d, $J = 5.2$ Hz, 1H, CH), 5.05 (dd, $J = 5.2$ Hz, $J' = 1.6$ Hz, 1H, CH=), 6.18 (b, 2H, NH_2), 6.81 (d, $J = 8.4$ Hz, 2H, ArH), 7.16 (d, $J = 8.4$ Hz, 2H, ArH), 7.32–7.37 (m, 3H, ArH), 7.48–7.53 (m, 2H, ArH), 8.28 (b, 1H, NH), 10.24 (b, 1H, NH). Anal. calcd. for $C_{20}H_{18}N_4O_2$: C, 69.35; H, 5.24; N, 16.17. Found: C, 69.20; H, 5.38; N, 16.22.

ACKNOWLEDGMENTS

We are grateful to the Natural Science Foundation (06AXL010) of Xuzhou Normal University for financial support.

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