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Synthesis of new pyrido[2,3-*d*]pyrimidin-5-one, pyrido[2,3-*d*]pyrimidin-7-one, and pyrimidino[4,5-*d*][1,3]oxazine derivatives from 5-acetyl-4-aminopyrimidines

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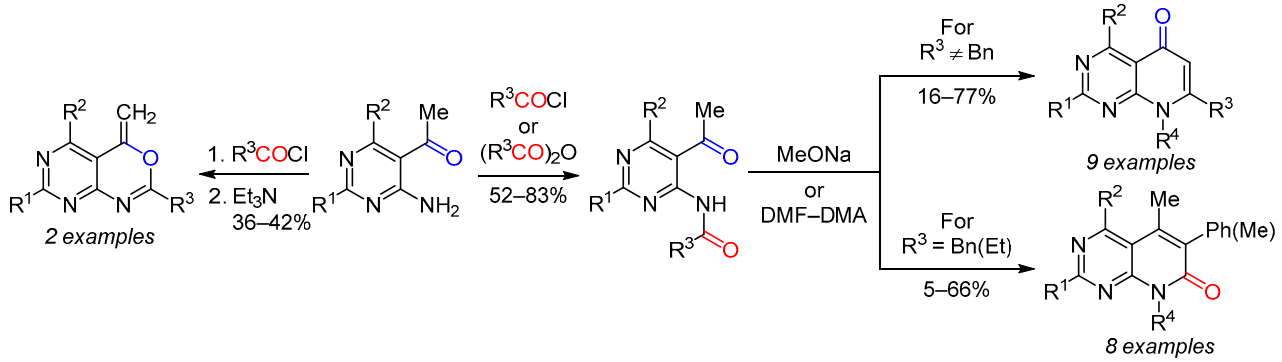


Methods were developed for the synthesis of new pyrido[2,3-*d*]pyrimidine and pyrimidino[4,5-*d*][1,3]oxazine derivatives. When heated under reflux with MeONa in BuOH, 5-acetyl-4-aminopyrimidines, acylated with carboxylic anhydrides or acid chlorides, are transformed into pyrido[2,3-*d*]pyrimidin-5-one derivatives, i.e., the acetyl methyl group and the amide carbonyl moiety are involved in the cyclization. In the presence of an activated CH_2 group (e.g., $PhCH_2$) in the amide moiety, the cyclization involves this group and the acetyl carbonyl giving rise to pyrido[2,3-*d*]pyrimidin-7-one derivatives. The reaction of 5-acetyl-4-aminopyrimidines with carboxylic acid chlorides under reflux in xylene followed by addition of a base affords pyrimidino[4,5-*d*][1,3]oxazines.

Keywords: 5-acetyl-4-aminopyrimidines, pyrido[2,3-*d*]pyrimidin-5-ones, pyrido[2,3-*d*]pyrimidin-7-ones, pyrimidino[4,5-*d*][1,3]oxazines, acylation, base-catalyzed cyclization.

The construction of molecules containing heterocycles, which are linked directly or *via* a spacer, as well as fused heterocycles, and the further evaluation of their chemical properties and biological activity are a rapidly growing area of organic synthesis.[1] Pyrido[2,3-*d*]pyrimidines comprise one of the most important classes of fused heterocyclic systems[2–4] due to a wide range of biological activity. Compounds of this class exhibit antiproliferative[5–7] antimicrobial,[8–10] anti-inflammatory and analgesic,[11,12] hypotensive,[13] and antihistaminic[14] activities. The compound API-1 belonging to pyrido[2,3-*d*]pyrimidin-5-one derivatives is a promising antiproliferative agent.[15] Among pyrido[2,3-*d*]pyrimidin-7-one derivatives, noteworthy are tyrosine kinase inhibitor TKI-28[16,17] and cyclin-dependent kinase (CDK4) inhibitors[17,18] (Fig. 1).

Methods for the synthesis, biological activities, and application of pyrido[2,3-*d*]pyrimidines are considered in

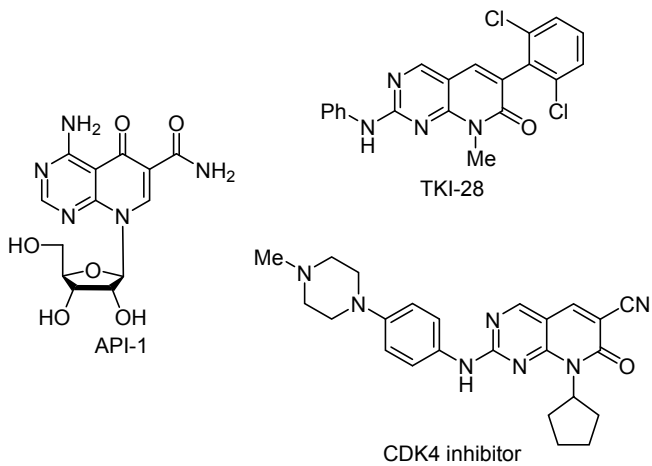
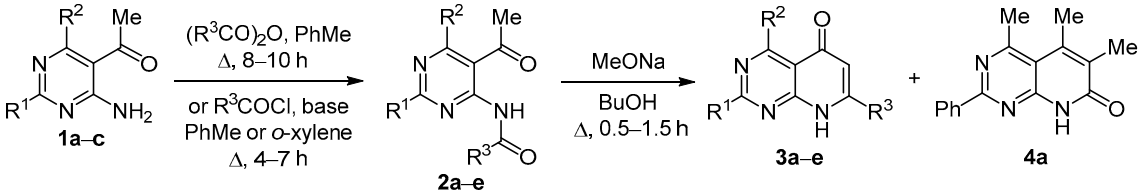


Figure 1. Biologically active compounds with pyrido[2,3-*d*]-pyrimidinone core.

Table 1. Synthesis of compounds **2a–e**, **3a–e**, **4a**



Compound	R^1	R^2	R^3	Product	Yield, %	Product	Yield, %	Product	Yield, %
1a	Ph	Me	Et	**2a**	83	**3a**	60	**4a**	5
1a	Ph	Me	*i*-Pr	**2b**	78	**3b**	54	–	–
1b	Me	Ph	*i*-Pr	**2c**	63	**3c**	35	–	–
1a	Ph	Me	2-Thienyl	**2d**	56	**3d**	77	–	–
1c	Cyclopropyl	Me	Cyclopropyl	**2e**	52	**3e**	31	–	–

detail in a recent review,[17] which also includes our studies.[19–23] The Gould–Jacobs reaction[24] is most commonly used in the synthesis of pyrido[2,3-*d*]pyrimidin-5-ones. This reaction involves the condensation of 6-amino-pyrimidines with ethoxymethylenemalonic ester followed by the cyclization at position 5 of the pyrimidine ring at high temperature (250°C in a mixture of diphenyl oxide and biphenyl). However, this reaction is applicable only to pyrimidines containing electron-donating substituents at position 4 (NR_2, OMe, OH), which significantly limits the range of possible products. Methods for the synthesis of pyrido[2,3-*d*]pyrimidin-7-one derivatives include the reaction of 5-formyl-4-methylaminopyrimidines with arylacetonitriles followed by hydrolysis of the 7-imino group,[16] the reaction of 4-amino-5-formylpyrimidines with cyanoacetic ester,[25] the reaction of 1,3-dialkyl-5-formyl-uracil with acetoacetamide,[26] the three-component reaction of 6-amino-2-(methylsulfanyl)pyrimidin-4(3*H*)-one with benzaldehydes and cyanoacetate,[27] and the palladium-catalyzed cross coupling of 5-iodopyrimidin-4(3*H*)-ones with acrylate, methacrylate, or crotonate followed by the treatment with $POCl_3$ and NH_3.[28]

Previously, we have shown that 5-acetyl-4-amino-pyrimidines (AAPs), which are easily produced by the $Ni(OAc)_2$-promoted reaction of acetylacetone or benzoyl-acetone with *N*-cyanoamidine,[19,29] can be efficiently used to construct the pyrido[2,3-*d*]pyrimidine system.[19–22,30,31] Thus, the condensation of AAPs with DMF–DMA or dimethylacetamide dimethyl acetal at the amino group followed by the cyclization affords pyrido[2,3-*d*]pyrimidin-5(8*H*)-ones.[19,31,32] The condensation with diethyl oxalate was employed to prepare 5-oxo-5,8-dihydropyrido[2,3-*d*]-pyrimidine-7-carboxylates.[20] It should be emphasized that the base-catalyzed annulation of the pyridine ring occurs with the participation of the acetyl methyl group of the starting AAP.

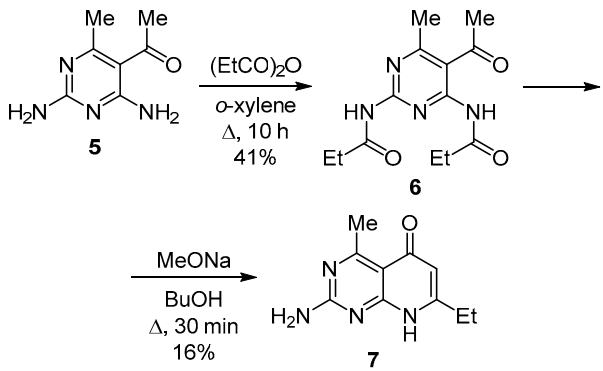
As part of our research, we examined the possibility of performing the cyclization of *N*-acylated AAPs under basic conditions, which would lead to pyrido[2,3-*d*]pyrimidin-5-ones bearing various substituents at position C-7.

5-Acetyl-4-aminopyrimidines **1a–c** were acylated by both carboxylic anhydrides and acid chlorides to form acyl-aminopyrimidines **2a–e** (Table 1) in 52–83% yields. Propionic and isobutyric anhydrides, 2-thiophenecarbonyl chloride, and cyclopropyl carbonyl chloride were used as acylating agents in the presence of Et_3N or DIPEA as bases. The acylation of pyrimidines **1a–c** requires rather drastic conditions, prolonged heating at reflux in PhMe or *o*-xylene and an excess of the acylating agent.

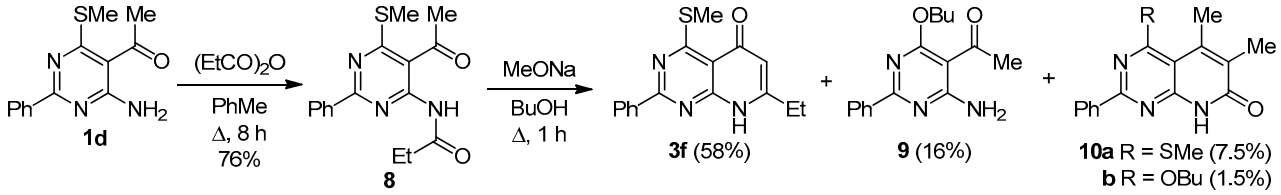
We found that heating of pyrimidines **2a–e** in BuOH at reflux in the presence of MeONa affords pyrido[2,3-*d*]-pyrimidin-5-ones **3a–e** in 31–77% yields (Table 1), i.e., the cyclization involves the methyl group of the acetyl moiety and the amide carbonyl group. The reaction with pyrimidine **2a** also produced pyrido[2,3-*d*]pyrimidin-7-one **4a** as a byproduct in 5% yield, the formation of which occurs *via* the cyclization of the amide CH_2 group at the acetyl carbonyl group. The reaction is accompanied by a side process, resulting in a decrease in yield of the target products. This process involves the deacylation of compounds **2a–e** to form starting pyrimidines **1a–c** and the subsequent Friedlander self-condensation[20] of the latter, which was confirmed by mass spectrometry.

Then we examined the possibility of preparing 2-amino-pyridopyrimidin-5-one from diaminopyrimidine **5**. For this purpose, the latter compound was transformed into compound **6** followed by cyclization into pyridopyrimidin-5-one **7** in 16% yield under the developed conditions (Scheme 1). In this reaction, the starting compound **5** was isolated as the major product in 56% yield, whereas its dimer as the Friedlander product and pyridopyrimidin-

Scheme 1. Synthesis of 2-amino-7-ethyl-4-methylpyridopyrimidin-5(8*H*)-one (**7**)



Scheme 2. Transformation of *N*-[5-acetyl-6-(methylsulfanyl)-2-phenylpyrimidin-4-yl]propanamide (**8**)



7-one, related to compound **4a**, were not detected. Compound **7** is readily soluble in H_2O, MeOH, and BuOH, which interferes with its isolation.

The acylation of 4-(methylsulfanyl)pyrimidine **1d** can be used to prepare heterocycle **8**. Under standard conditions (heating in BuOH at reflux in the presence of MeONa), the reaction of compound **8** affords pyrido-pyrimidin-5-one **3f** as the major product (as in the case of the transformation of compounds **2**) in 58% yield with the retention of the methylsulfanyl group (Scheme 2). This reaction also gives 4-butoxypyrimidine **9** (16% yield), which is produced by the deacylation and subsequent replacement of the methylsulfanyl group by BuO group, and also 4-(methylsulfanyl)pyridopyrimidin-7-one **10a**. Besides, the reaction gave 4-butoxypyridopyrimidin-7-one **10b**, which was detected as an impurity in the ^{1}H NMR spectra of compound **10a** (**10a**/**10b** ratio 5:1 according to the ^{1}H NMR data, yield of compound **10b** 1.5%). The possibility of replacing the SMe group at the pyrimidine ring after its oxidation makes compound **3f** useful to prepare other pyrido[2,3-*d*]pyrimidin-5-one derivatives.

Previously,[19] we have reported the transformation of 5-acetyl-4-benzoylaminopyrimidines (related to compounds **2**) to pyridopyrimidin-5-ones (related to compounds **3**). Therefore, this reaction has a general character and can be applied to synthesize pyrido[2,3-*d*]pyrimidin-5-ones containing alkyl, aryl, or hetaryl substituents at C-7 position. This reaction with MeONa in refluxing MeOH did not afford products **3** at all and led only to deacylation.

The structures of compounds **2a–h**, **3a–f**, **6**, **7**, **8**, and **9** were proved by the IR, NMR (^{1}H, ^{13}C, ^{1}H–^{13}C HMBC) spectral data and mass spectra. In a solution, heterocycles **3a–f** exist in the pyridone form. Only compound **3e** bearing the cyclopropyl substituent at position C-7 partially (12%) exists in the hydroxypyridine form. Signals of the pyridone form in the ^{1}H and ^{13}C NMR spectra in $CDCl_3$: 3.07 ppm (Me group), 6.00 ppm (H-6), 24.5 ppm (Me group), 110.6 ppm

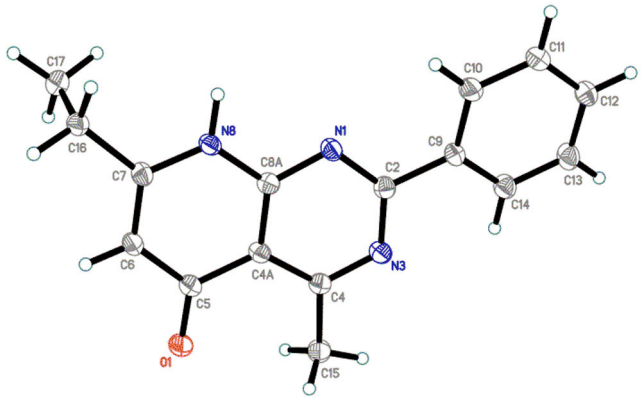
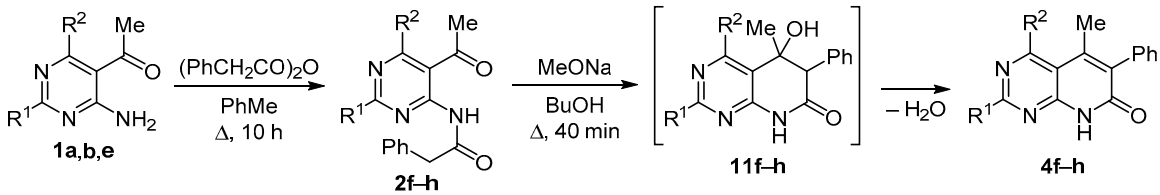


Figure 2. Molecular structure of compound **3a** with displacement ellipsoids drawn at the 50% probability level.

(C-6), 179.1 ppm (C=O); signals of the hydroxypyridine form: 3.12 ppm (Me group), 7.33 ppm (H-6), 28.0 ppm (Me group), 122.5 ppm (C-6). The structure of compound **3a** was established by X-ray diffraction (Fig. 2).

Acylation of starting AAPs **1a**,**b**,**e** with phenylacetic anhydride gave pyrimidines **2f–h**, which by refluxing in BuOH with MeONa were transformed into pyrido[2,3-*d*]-pyrimidin-7-ones **4f–h** in 48–66% yields (Table 2), while possible byproducts – pyrido[2,3-*d*]pyrimidin-5-ones **3** were not detected. This cyclization occurs *via* the attack of the activated CH_2 group of the amide moiety on the acetyl carbonyl. The formation of heterocycles **4f–h** proceeds through intermediates **11f–h**. This is evidenced by the fact that pyrimidine **2h** was completely transformed into intermediate **11h** within 5 days in DMSO-d_6. The structures of compounds **2f–h** and **4f–h** were supported by the ^{1}H, ^{13}C, ^{1}H–^{13}C HMBC NMR experiments. Compound **11h** contains two asymmetric centers, which is manifested in the ^{1}H and ^{13}C NMR spectra (two sets of the signals of H-6, Me group at C-5, Me group at C-4, and OH in the ^{1}H NMR spectrum and of Me group at C-5 and C-6 in the

Table 2. Synthesis of pyrido[2,3-*d*]pyrimidin-7(8*H*)-ones **4f–h**



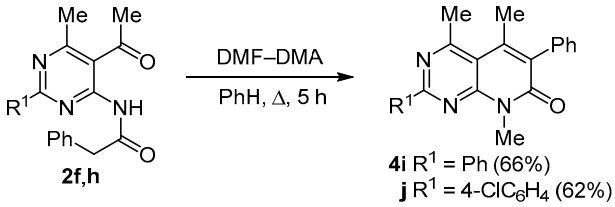
Compound	R^1	R^2	Product	Yield, %	Product	Yield, %	Product	Yield, %
1a	Ph	Me	**2f**	47	**11f**	–	**4f**	51
1b	Me	Ph	**2g**	78	**11g**	–	**4g**	48
1e	4-ClC_6H_4	Me	**2h**	43	**11h**	–	**4h**	65

^{13}C NMR spectrum). In the NOESY experiment of compound **11h** a correlation was observed between the *ortho* protons of the Ph group at C-6 and protons of the Me group at C-5 from the major diastereomer (88%), i.e., these groups in the major isomer are in close proximity.

Previously,[30] we have found that the heating of AAPs **1** with β-keto esters or malonic ester to 180–190°C resulted in the formation of 6-acyl-5-methylpyrido[2,3-*d*]pyrimidin-7(8*H*)-ones and 7-oxo-7,8-dihydropyrido[2,3-*d*]pyrimidine-6-carboxylates, respectively. Therefore, we demonstrated that AAPs **1a**,**b**,**e** can be used also to synthesize pyrido[2,3-*d*]-pyrimidin-7-one derivatives **4f**–**h**.

In a number of our previous studies, we showed that pyrido[2,3-*d*]pyrimidin-5-one derivatives can also be synthesized by the condensation of DMF–DMA at the acetyl group of 5-acetyl-4-aminopyrimidines followed by the pyridine ring closure involving the amino group.[33,34] Therefore, we examined the reaction of 5-acetyl-4-acylaminopyrimidines **2** with DMF–DMA. The heating of pyrimidines **2f**,**h** at reflux with DMF–DMA in PhH did not lead to the condensation at the acetyl group, but resulted in the formation of pyrido[2,3-*d*]pyrimidin-7-ones **4i**,**j** in 62–66% yields (Scheme 3).

Scheme 3. Transformation of 5-acetyl-4-acylamino-pyrimidines **2f**,**h**



This is attributed to the fact that DMF–DMA exists in solution in equilibrium with the ambident cation and the methoxide anion,[35,36] and the latter promotes the cyclization of pyrimidines **2f**,**h** to products **4f**,**h**. Besides, DMF–DMA is a good methylating agent, which leads to the transformation of compounds **4f**,**h** into compounds **4i**,**j** (the mechanism of alkylation with amide acetals was reported previously[35]). Methylated compounds **4i**,**j** are easily purified from an impurity of non-methylated bicyclic compounds **4f**,**h** using MeCN (compounds **4i**,**j**, unlike **4f**,**h**, are readily soluble in MeCN). The structure of compound **4i** was established by X-ray diffraction (Fig. 3).

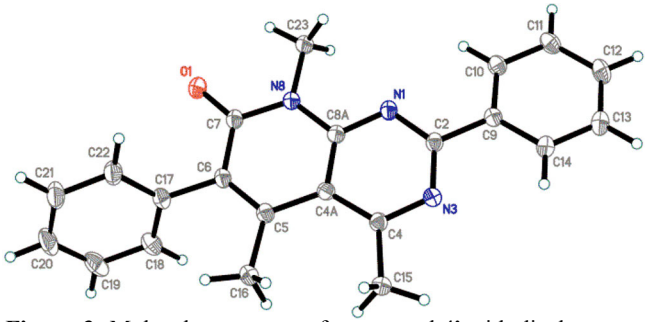
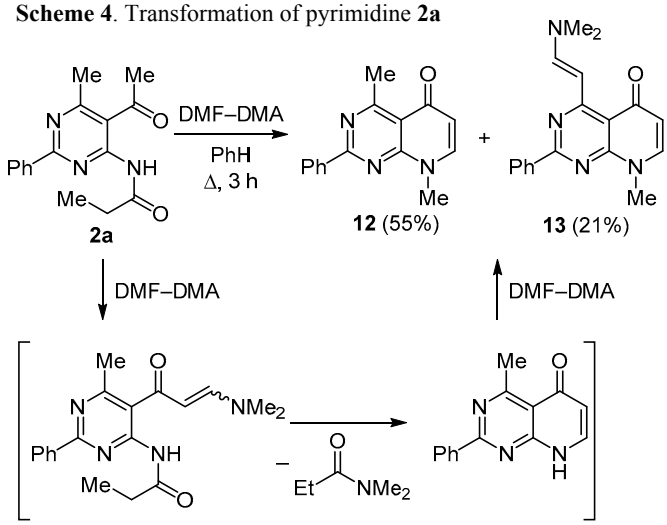


Figure 3. Molecular structure of compound **4i** with displacement ellipsoids drawn at the 50% probability level.

The heating of pyrimidine **2a** under reflux with DMF–DMA in PhH afforded a mixture of compounds **12** and **13**, whereas pyrido[2,3-*d*]pyrimidin-5-one **3a** was not detected. This reaction involves the condensation of DMF–DMA at the methyl group of the acetyl moiety, the cyclization to pyrido[2,3-*d*]pyrimidin-5-one accompanied by the elimination of *N*,*N*-dimethylpropionamide, *N*-methylation, and condensation at the methyl group of compound **12** (Scheme 4).

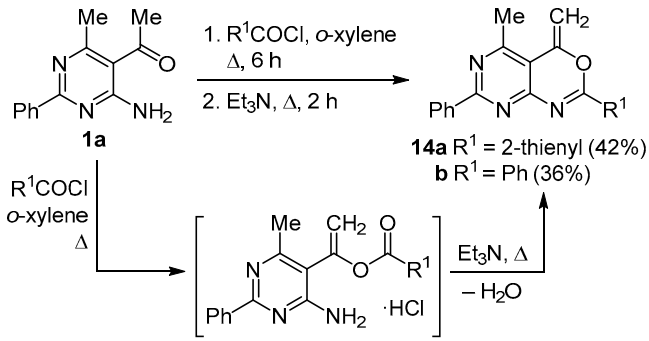
Scheme 4. Transformation of pyrimidine **2a**



The acylation of pyrimidine **1a** with thiophenecarbonyl chloride in standard conditions afforded 5-methyl-4-methylidene-7-phenyl-2-(thiophen-2-yl)-4*H*-pyrimido[4,5-*d*][1,3]-oxazine (**14a**) as a byproduct (was detected in ^{1}H NMR of crude reaction mixture) (Scheme 5).

Hence, we examined the possibility of preparing other structurally similar compounds. Attempts to transform acylated pyrimidine **2d** into compound **14a** failed (the heating of compound **2d** in xylene under reflux did not lead to any changes; upon the addition of *p*-TsOH, the respective salt was isolated). This is evidence that the formation of acylated compound **2d** and heterocycle **14a** are independent processes. Nevertheless, we succeeded in developing a method for the preparation of pyrimido[4,5-*d*][1,3]oxazines based on the heating of pyrimidine **1a** with carboxylic acid chlorides under reflux in xylene followed by the treatment with a base. Thus, compounds **14a**,**b** were synthesized from AAP **1a** and thiophenecarbonyl chloride or benzoyl chloride (Scheme 5).

Scheme 5. Synthesis of pyrimido[4,5-*d*][1,3]oxazines **14a**,**b**



Apparently, in the absence of a base, the acylation of pyrimidine hydrochloride **1a** at the NH_2 group is hindered, and this compound undergoes mainly *O*-acylation of the acetyl moiety. The heating of compound **14a** under reflux in MeOH with MeONa resulted in its rearrangement into pyrido[2,3-*d*]pyrimidin-5-one **3d**. The structures of compounds **14a**,**b** were proved by the NMR (^{1}H, ^{13}C, ^{1}H–^{13}C HMBC) spectral data and mass spectra. It is worth noting that compounds of this class exhibit anticoagulant activity.[37]

To conclude, we demonstrated that pyrido[2,3-*d*]-pyrimidin-5-ones and pyrido[2,3-*d*]pyrimidin-7-ones, as well as pyrimido[4,5-*d*][1,3]oxazines, can be synthesized through the acylation of 5-acetyl-4-aminopyrimidines.

Experimental

IR spectra were recorded on a Bruker Alpha spectrometer as KBr pellets or in $CHCl_3$. ^{1}H and ^{13}C NMR were recorded on Bruker AV-600 (600 and 151 MHz, respectively), Bruker DRX-500 (^{1}H NMR, 500 MHz), Bruker AV-400 (400 and 101 MHz, respectively), Bruker AM-300 (300 and 76 MHz, respectively), and Bruker WM-250 (^{1}H NMR, 250 MHz) spectrometers in $CDCl_3$ or DMSO-d_6. Internal standards were signals of the solvents ($CDCl_3$: 7.27 ppm for ^{1}H nuclei and 77.0 ppm for ^{13}C nuclei; DMSO-d_6: 2.50 ppm for ^{1}H nuclei and 39.5 ppm for ^{13}C nuclei). The assignment of the signals in the NMR spectra was based on the 2D NMR data. NOESY, ^{1}H–^{13}C HSQC, ^{1}H–^{13}C HMBC spectra were recorded on Bruker AV-600 (600 and 151 MHz, respectively) and Bruker AV-400 (400 and 101 MHz, respectively) spectrometers, using the standard procedure with gradient separation of the signal. High-resolution mass spectra were obtained on a Bruker MicroTOF mass spectrometer by electrospray ionization (ESI) using Q-TOF detection. The melting points were determined on a Kofler hot stage apparatus and are uncorrected. TLC was performed using Silicagel 60 F_{254} plates. The chromatograms were visualized with an UV lamp (365 nm). Column chromatography was carried out on silica gel 60 (0.063–0.200 mm, Merck).

Phenylacetic anhydride,[38] ethyl cyclopropanecarbimidate hydrochloride,[39] and pyrimidines **1a**,[29] **1b**,[19] **1e**,[20] **1d**[32], **5**[40] were prepared according to the literature.

1-(4-Amino-2-cyclopropyl-6-methylpyrimidin-5-yl)-ethan-1-one (1c). *N*'-Cyanocyclopropanecarboximidamide was prepared according to the method for *N*-cyanoamidine preparation.[41] A solution of K_2CO_3 (4.58 g, 33.0 mmol) in H_2O (25 ml) was added to a suspension of ethyl cyclopropanecarbimidate hydrochloride (3.00 g, 22.0 mmol) in Et_2O (25 ml); the mixture was shaken, organic layer was separated, dried over K_2CO_3, and evaporated. Residue was dissolved in MeOH (10 ml), and cyanamide (0.93 g, 22.0 mmol) was added. The resulting mixture was stirred at room temperature for 6 h. MeOH was evaporated, the obtained residue was washed with PhH–hexane. Yield 1.58 g (66%), white solid, mp 131–132°C. IR spectrum (KBr), ν, cm^{-1}: 3300 (NH), 3124 (NH), 2224 (CN), 2180 (CN), 1680, 1548, 1452, 1344, 1208, 1200, 1116, 1064, 1044, 1008, 920, 824, 784, 752, 708, 692, 668. ^{1}H NMR spectrum (300 MHz, DMSO-d_6), δ, ppm: 0.82–0.98 (4H, m, $2CH_2$); 1.60–1.70 (1H, m, CH); 7.88 (1H, br. s, NH); 8.52 (1H, br. s, NH). ^{13}C NMR spectrum (76 MHz, DMSO-d_6), δ, ppm: 8.7 ($2CH_2$); 13.9 (CH); 116.8 (C≡N); 177.1 (C=N).

A mixture of *N*'-cyanocyclopropanecarboximidamide (0.94 g, 8.6 mmol) and $Ni(OAc)_2$ (1.52 g, 8.6 mmol) in acetylacetone (10 ml) was stirred at 140°C for 3.5 h. Then acetylacetone was removed under reduced pressure and the crude product was purified by column chromatography (SiO_2, $CHCl_3$). The product was additionally purified by crystallization from petroleum ether. Yield 0.47 g (29%), white solid, mp 134–135°C, R_f 0.46 ($CHCl_3$–MeOH, 30:1). IR spectrum (KBr), ν, cm^{-1}: 3384 (NH), 3300 (NH), 3187 (NH), 3007, 1665 (C=O), 1622, 1539, 1446, 1388, 1356, 1330, 1261, 1240, 1091, 1068, 1028, 953, 878, 818, 801, 681, 623. ^{1}H NMR spectrum (600 MHz, $CDCl_3$), δ, ppm: 0.93–0.98 (2H, m, CH_2); 1.07–1.12 (2H, m, CH_2); 1.95–2.00 (1H, m, CH); 2.55 (3H, s, CH_3CO); 2.59 (3H, s, CH_3); 6.72 (2H, br. s, NH_2). ^{13}C NMR spectrum (151 MHz, $CDCl_3$), δ, ppm: 10.3 ($2CH_2$); 17.9 (CH); 26.4 (CH_3); 33.1 ($\underline{C}H_3CO$); 111.4 (C-5); 162.3 (C-4); 166.6 (C-6); 172.4 (C-2); 201.2 (CO). Found, *m*/*z*: 192.1137 $[M+H]^+$. $C_{10}H_{14}N_3O$. Calculated, *m*/*z*: 192.1131.

***N*-(5-Acetyl-6-methyl-2-phenylpyrimidin-4-yl)propanamide (2a)**. A mixture of pyrimidine **1a** (128 mg, 0.56 mmol) and propionic anhydride (0.15 ml, 1.12 mmol) in PhMe (4 ml) was refluxed for 10 h and then cooled to room temperature. Petroleum ether (10 ml) was added to the reaction mixture, and the precipitate was filtered off. Yield 133 mg (83%), white solid, mp 137–138°C. IR spectrum (KBr), ν, cm^{-1}: 3060, 2978, 2939, 1692 (C=O), 1574, 1533, 1504, 1427, 1392, 1356, 1254, 1177, 1080, 1027, 934, 771, 692, 568. ^{1}H NMR spectrum (400 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 1.28 (3H, t, *J* = 7.0, $C\underline{H}_3CH_2$); 2.60 (3H, s, CH_3CO); 2.67 (2H, q, *J* = 7.0, CH_2); 2.71 (3H, s, CH_3); 7.48–7.54 (3H, m, H Ar); 8.40 (2H, m, H Ar); 8.79 (1H, s, NH). ^{13}C NMR spectrum (101 MHz, $CDCl_3$), δ, ppm: 8.9 ($\underline{C}H_3CH_2$); 24.7 (CH_3); 30.9 (CH_2); 31.6 ($\underline{C}H_3CO$); 119.9 (C-5); 128.5 (2CH Ar); 128.6 (2CH Ar); 131.4 (CH Ar); 136.5 (C Ar); 154.1 (C-4); 163.6 (C-2); 166.0 (C-6); 173.3 (NCO); 200.6 (CO). Found, *m*/*z*: 284.1393 $[M+H]^+$. $C_{16}H_{18}N_3O_2$. Calculated, *m*/*z*: 284.1394.

***N*-(5-Acetyl-6-methyl-2-phenylpyrimidin-4-yl)-2-methylpropanamide (2b)**. A mixture of pyrimidine **1a** (130 mg, 0.57 mmol) and isobutyric anhydride (0.19 ml, 1.15 mmol) in PhMe (4 ml) was refluxed for 9 h and then cooled to room temperature. Petroleum ether (30 ml) was added to the reaction mixture, precipitate was filtered off. The filtrate was concentrated, and the residue was dissolved in PhH (1 ml). Petroleum ether (10 ml) was added to the mixture, and the precipitate of the target product was filtered off. Yield 132 mg (78%), white solid, mp 162–163°C (PhH–hexane). IR spectrum (KBr), ν, cm^{-1}: 3296 (NH), 2937, 2932, 2874, 1693 (C=O), 1679 (C=O), 1577, 1535, 1503, 1393, 1257, 1229, 1198, 1168, 1130, 1102, 1031, 952, 772, 701, 648, 582. ^{1}H NMR spectrum (600 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 1.09 (6H, d, *J* = 6.8, $2CH_3$); 2.35 (3H, s, CH_3CO); 2.56 (3H, s, CH_3); 2.78–2.85 (1H, m, CH); 7.52–7.58 (3H, m, H Ar); 8.39 (2H, d, *J* = 7.9, H Ar); 10.93 (1H, s, NH). ^{13}C NMR spectrum (151 MHz, DMSO-d_6),

δ, ppm: 18.7 ($2CH_3$); 23.5 (CH_3); 29.9 ($\underline{C}H_3CO$); 34.1 (CH); 122.4 (C-5); 127.9 (2CH Ar); 128.6 (2CH Ar); 131.2 (CH Ar); 136.2 (C Ar); 154.2 (C-4); 162.3 (C-2); 165.0 (C-6); 176.6 (NCO); 197.8 (CO). Found, *m*/*z*: 298.1554 $[M+H]^+$. $C_{17}H_{20}N_3O_2$. Calculated, *m*/*z*: 298.1550.

***N*-(5-Acetyl-2-methyl-6-phenylpyrimidin-4-yl)-2-methylpropanamide (2c)**. A mixture of pyrimidine **1b** (102 mg, 0.45 mmol) and isobutyric anhydride (0.30 ml, 1.80 mmol) in PhMe (4 ml) was refluxed for 8 h and then cooled to room temperature. PhMe was removed under reduced pressure, and the crude product was purified by column chromatography (SiO_2, $CHCl_3$; $CHCl_3$–MeOH, 150:1). Yield 84 mg (63%), colorless solid, mp 130–131°C, R_f 0.52 ($CHCl_3$–MeOH, 25:1). IR spectrum (KBr), ν, cm^{-1}: 3285 (NH), 3262 (NH), 2973, 2932, 2875, 1702 (C=O), 1683 (C=O), 1573, 1532, 1491, 1446, 1404, 1381, 1353, 1249, 1204, 1170, 1097, 1067, 1031, 940, 858, 813, 766, 704, 668, 639, 609, 576, 492, 453. ^{1}H NMR spectrum (600 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 1.03 (6H, d, *J* = 6.9, $2CH_3$); 1.91 (3H, s, CH_3CO); 2.61 (3H, s, CH_3); 2.68–2.74 (1H, m, CH); 7.40 (2H, d, *J* = 6.9, H Ar); 7.48–7.55 (3H, m, H Ar); 10.85 (1H, s, NH). ^{13}C NMR spectrum (151 MHz, DMSO-d_6), δ, ppm: 18.5 ($2CH_3$); 25.3 (CH_3); 30.5 ($\underline{C}H_3CO$); 34.0 (CH); 122.4 (C-5); 128.4 (2CH Ar); 128.5 (2CH Ar); 129.7 (CH Ar); 138.1 (C Ar); 154.3 (C-4); 163.8 (C-6); 166.6 (C-2); 176.2 (NCO); 199.1 (CO). Found, *m*/*z*: 298.1548 $[M+H]^+$. $C_{17}H_{20}N_3O_2$. Calculated, *m*/*z*: 298.1550.

***N*-(5-Acetyl-6-methyl-2-phenylpyrimidin-4-yl)thiophene-2-carboxamide (2d)**. A mixture of pyrimidine **1a** (200 mg, 0.90 mmol), 2-thiophenecarbonyl chloride (0.19 ml, 1.80 mmol), and Et_3N (0.28 ml, 2.00 mmol) in *o*-xylene (5 ml) was refluxed for 4 h and then cooled to room temperature. The precipitate of the target compound was filtered off and washed with H_2O. The filtrate was concentrated, and the crude product was purified by column chromatography (SiO_2, $CHCl_3$; $CHCl_3$–MeOH, 100:1) to provide additional portion of compound **2d**. Yield 167 mg (56%), colorless solid, mp 171–172°C (PhH–hexane), R_f 0.22 (PhH–EtOH, 40:1). IR spectrum (KBr), ν, cm^{-1}: 3308 (NH), 1688 (C=O), 1648 (C=O), 1576, 1520, 1488, 1420, 1392, 1356, 1284, 1248, 1140, 1100, 984, 856, 768, 704. ^{1}H NMR spectrum (600 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 2.65 (3H, s, CH_3CO); 2.73 (3H, s, CH_3); 7.17 (1H, dd, *J* = 4.5, *J* = 2.7, CH Het); 7.46–7.55 (3H, m, H Ar); 7.64 (1H, d, *J* = 4.5, H Het); 7.80 (1H, d, *J* = 2.7, H Het); 8.48 (2H, d, *J* = 7.0, H Ar); 9.71 (1H, br. s, NH). ^{13}C NMR spectrum (151 MHz, $CDCl_3$), δ, ppm: 25.0 (CH_3); 31.6 ($\underline{C}H_3CO$); 119.9 (C-5); 128.1 (CH Het); 128.6 (2CH Ar); 128.7 (2CH Ar); 130.2 (CH Het); 131.5 (CH Ar); 132.8 (CH Het); 136.4 (C Ar); 138.2 (C Het); 154.5 (C-4); 159.8 (NCO); 163.9 (C-2); 166.4 (C-6); 201.0 (CO). Found, *m*/*z*: 338.0963 $[M+H]^+$. $C_{18}H_{16}N_3O_2S$. Calculated, *m*/*z*: 338.0958.

***N*-(5-Acetyl-2-cyclopropyl-6-methylpyrimidin-4-yl)-cyclopropanecarboxamide (2e)**. A mixture of pyrimidine **1c** (200 mg, 1.05 mmol), cyclopropylcarbonyl chloride (0.19 ml, 2.10 mmol), and DIPEA (0.48 ml, 2.63 mmol) in PhMe (10 ml) was refluxed for 7 h and then cooled to room temperature. PhH (30 ml) was added, and the reaction mixture was washed with H_2O (3×13 ml). The organic layer was dried over Na_2SO_4, concentrated. The crude product was purified by column chromatography (SiO_2, $CHCl_3$; $CHCl_3$–MeOH, 100:1). Yield 140 mg (52%), colorless solid, mp 108–109°C (hexane), R_f 0.54 ($CHCl_3$–MeOH, 30:1). IR spectrum (KBr), ν, cm^{-1}: 3293 (NH), 1691 (C=O), 1670 (C=O), 1584, 1543, 1502, 1437, 1374, 1294, 1242, 1220, 1187, 1098, 1059, 1037, 1023, 982, 945, 881, 867, 818, 704, 660, 586. ^{1}H NMR spectrum (400 MHz, $CDCl_3$), δ, ppm: 0.90–0.96 (2H, m, CH_2); 1.02–1.07 (2H, m, CH_2); 1.07–1.15 (4H, m, $2CH_2$); 1.77–1.84 (1H, m, CH); 2.10–2.17 (1H, m, CHCO); 2.47 (3H, s, CH_3CO); 2.56 (3H, s, CH_3); 8.81 (1H, s, NH). ^{13}C NMR spectrum (101 MHz, $CDCl_3$), δ, ppm: 9.2 ($2CH_2$); 10.9 ($2CH_2$); 15.6 ($\underline{C}HCO$); 18.0 (CH); 24.1 (CH_3); 31.1 ($\underline{C}H_3CO$); 119.8 (C-5); 153.4 (C-4); 165.5 (C-6); 171.7 (NCO); 173.2 (C-2); 200.0 (CO). Found, *m*/*z*: 260.1398 $[M+H]^+$. $C_{14}H_{18}N_3O_2$. Calculated, *m*/*z*: 260.1394.

Synthesis of *N*-(5-acetylpyrimidin-4-yl)-2-phenylacetamides 2f–h (General method). A mixture of pyrimidine **1a**,**b**,**e** (0.60 g, 2.64 mmol) and phenylacetic anhydride (1.36 g, 5.35 mmol) in PhMe (9 ml) was refluxed for 10 h and then cooled to room temperature. Petroleum ether (10 ml) was added, and the precipitate that formed was filtered off.

***N*-(5-Acetyl-6-methyl-2-phenylpyrimidin-4-yl)-2-phenylacetamide (2f)**. Yield 0.43 g (47%), white solid, mp 174–175°C (PhH–hexane). ^{1}H NMR spectrum (250 MHz, $CDCl_3$), δ, ppm: 2.52 (3H, s, CH_3); 2.67 (3H, s, CH_3); 3.88 (2H, s, CH_2); 7.30–7.50 (8H, m, H Ar); 8.35–8.42 (2H, m, H Ar); 8.65 (1H, s, NH). Found, *m*/*z*: 346.1543 $[M+H]^+$. $C_{21}H_{20}N_3O_2$. Calculated, *m*/*z*: 346.1550.

***N*-(5-Acetyl-2-methyl-6-phenylpyrimidin-4-yl)-2-phenylacetamide (2g)**. Yield 0.71 g (78%), white solid, mp 159–160°C (PhH–hexane). IR spectrum (KBr), ν, cm^{-1}: 3409, 3202, 3134, 3062, 3009, 1694 (C=O), 1661 (C=O), 1573, 1512, 1493, 1440, 1405, 1375, 1353, 1309, 1280, 1231, 1159, 1032, 970, 921, 880, 758, 728, 696, 560, 520. ^{1}H NMR spectrum (600 MHz, $CDCl_3$), δ, ppm: 1.92 (3H, s, CH_3CO); 2.74 (3H, s, CH_3); 3.97 (2H, s, CH_2); 7.33–7.37 (3H, m, H Ar); 7.38–7.42 (2H, m, H Ar); 7.46–7.50 (2H, m, H Ar); 7.51–7.55 (3H, m, H Ar); 9.43 (1H, s, NH). ^{13}C NMR spectrum (151 MHz, $CDCl_3$), δ, ppm: 26.2 (CH_3); 31.5 ($\underline{C}H_3CO$); 45.0 (CH_2); 117.5 (C-5); 127.6 (CH Ar); 129.0 (4CH Ar); 129.1 (2CH Ar); 129.6 (CH Ar); 130.8 (2CH Ar); 133.6 (C Ar); 138.2 (C Ar); 154.7 (C-4); 166.3 (C-6); 168.4 (C-2); 170.2 (NCO); 203.2 (CO). Found, *m*/*z*: 346.1539 $[M+H]^+$. $C_{21}H_{20}N_3O_2$. Calculated, *m*/*z*: 346.1550.

***N*-[5-Acetyl-2-(4-chlorophenyl)-6-methylpyrimidin-4-yl]-2-phenylacetamide (2h)**. Yield 0.37 g (43%), white solid, mp 203–204°C (PhH–hexane). IR spectrum (KBr), ν, cm^{-1}: 3280 (NH), 1690 (C=O), 1572, 1534, 1498, 1419, 1393, 1348, 1254, 1176, 1132, 1085, 1010, 969, 901, 846, 804, 779, 703, 629, 565. ^{1}H NMR spectrum (500 MHz, DMSO-d_6–CCl_4, 1:3), δ, ppm (*J*, Hz): 2.22 (3H, s, CH_3); 2.57 (3H, s, CH_3); 3.77 (2H, s, CH_2); 7.22 (1H, t, *J* = 7.2, H Ar); 7.29 (2H, t, *J* = 7.2, H Ar); 7.34 (2H, d, *J* = 7.2, H Ar); 7.48 (2H, d, *J* = 8.5, H Ar); 8.40 (2H, d, *J* = 8.5, H Ar); 10.94 (1H, s, NH). Found, *m*/*z*: 380.1151 $[M+H]^+$. $C_{21}H_{19}ClN_3O_2$. Calculated, *m*/*z*: 380.1160.

7-Ethyl-4-methyl-2-phenylpyrido[2,3-*d*]pyrimidin-5(8*H*)-one (3a). Pyrimidine **2a** (80 mg, 0.28 mmol) was added to a freshly prepared boiling solution of MeONa (30 mg, 0.56 mmol) in BuOH (5 ml). The reaction mixture was refluxed for 50 min and then cooled to room temperature. The precipitate was filtered off and suspended in H_2O (10 ml), AcOH (0.2 ml) was added, and the mixture was stirred for 15 min. The precipitate was filtered off and washed with H_2O (39 mg of compound **3a** was obtained). The BuOH solution (after the first filtration step) was concentrated, the residue was suspended in H_2O (10 ml), AcOH (0.2 ml) was added, and the mixture was stirred for 15 min. The precipitate was filtered off and sequentially washed with H_2O (10 ml), PhH (10 ml), and MeOH (5 ml). Obtained residue was purified by column chromatography (SiO_2, $CHCl_3$; $CHCl_3$–MeOH, 100:1, 5 mg of compound **3a** was obtained). Yield 44 mg (60%), colorless solid, mp 263–264°C (DMSO–H_2O), R_f 0.32 ($CHCl_3$–MeOH, 25:1). IR spectrum (KBr), ν, cm^{-1}: 3042, 2912, 2871, 2761, 1652 (C=O), 1623, 1593, 1581, 1568, 1540, 1503, 1453, 1422, 1397, 1357, 1279, 1251, 1151, 1087, 1061, 1019, 869, 856, 784, 725, 694, 629, 545, 471, 424. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 1.23 (3H, t, *J* = 6.6, $\underline{C}H_3CH_2$); 2.62 (2H, q, *J* = 6.6, CH_2); 2.99 (3H, s, CH_3); 6.03 (1H, s, H-6); 7.45–7.60 (3H, m, H Ar); 8.40–8.52 (2H, m, H Ar); 11.70 (1H, br. s, NH). ^{13}C NMR spectrum (101 MHz, DMSO-d_6), δ, ppm: 12.9 ($\underline{C}H_3CH_2$); 25.7 (CH_3); 26.3 (CH_2); 112.2 (C-6); 113.1 (C-4a); 128.8; 129.0 (4CH Ar); 131.6 (CH Ar); 137.1 (C Ar); 155.9 (C-7); 156.9 (C-8a); 162.9 (C-2); 171.0 (C-4); 178.8 (C-5). Found, *m*/*z*: 266.1281 $[M+H]^+$. $C_{16}H_{16}N_3O$. Calculated, *m*/*z*: 266.1288.

4,5,6-Trimethyl-2-phenylpyrido[2,3-*d*]pyrimidin-7(8*H*)-one (4a) was obtained as a byproduct during chromatographic separation of compound **3a**. Yield 4 mg (5%), white solid, mp 200–202°C (MeCN), R_f 0.54 ($CHCl_3$–MeOH, 25:1). IR spectrum (KBr), ν, cm^{-1}: 2922, 1642 (C=O), 1597, 1572, 1527, 1423, 1371, 1339, 1291, 1244, 1172, 1135, 1116, 1026, 908, 816, 778, 735, 701, 646, 597, 546. ^{1}H NMR spectrum (600 MHz, DMSO-d_6), δ, ppm: 2.12 (3H, s, 6-CH_3); 2.58 (3H, s, 5-CH_3); 2.94 (3H, s, 4-CH_3); 7.52–7.55 (3H, m, H Ar); 8.40–8.43 (2H, m, H Ar); 12.23 (1H, s, NH). ^{13}C NMR spectrum (151 MHz, DMSO-d_6), δ, ppm: 12.9 (6-CH_3); 19.7 (5-CH_3); 27.7 (4-CH_3); 111.4 (C-4a); 127.9 (2CH Ar); 128.6 (2CH Ar); 129.2 (C-6); 131.0 (CH Ar); 136.4 (C Ar); 142.0 (C-5); 153.8 (C-8a); 159.8 (C-2); 162.4 (C-7); 164.9 (C-4). Found, *m*/*z*: 266.1296 $[M+H]^+$. $C_{16}H_{16}N_3O$. Calculated, *m*/*z:* 266.1288.

7-Isopropyl-4-methyl-2-phenylpyrido[2,3-*d*]pyrimidin-5(8*H*)-one (3b). Pyrimidine **2b** (58 mg, 0.20 mmol) was added to a freshly prepared boiling solution of MeONa (22 mg, 0.40 mmol) in BuOH (4 ml). The mixture was refluxed for 40 min and cooled to room temperature, AcOH (0.1 ml) was added, and the mixture was stirred for 15 min. Reaction mixture was concentrated, and the residue was suspended in MeOH (3 ml) followed by filtration of precipitate. The obtained filtrate was concentrated. The crude product was purified by column chromatography (SiO_2, $CHCl_3$; $CHCl_3$–MeOH, 100:1). Yield 30 mg (54%), colorless solid, mp 225–226°C (MeCN), R_f 0.28 ($CHCl_3$–MeOH, 25:1). IR spectrum (KBr), ν, cm^{-1}: 3068, 2973, 1647 (C=O), 1627, 1579, 1538, 1451, 1404, 1364, 1352, 1316, 1268, 1244, 1175, 1155, 1049, 1069, 1029, 862, 808, 782, 725, 695, 521. ^{1}H NMR spectrum (600 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 1.26 (6H, d, *J* = 7.0, $2CH_3$); 2.88–2.92 (1H, m, CH); 2.96 (3H, s, CH_3); 6.05 (1H, s, H-6); 7.52–7.58 (3H, m, H Ar); 8.47 (2H, d, *J* = 8.1, H Ar); 12.00 (1H, br. s, NH). ^{13}C NMR spectrum (151 MHz, DMSO-d_6), δ, ppm: 21.1 ($2CH_3$); 25.5 (CH_3); 31.5 (CH); 109.8 (C-6); 112.7 (C-4a); 128.3 (2CH Ar); 128.6 (2CH Ar); 131.4 (CH Ar); 136.5 (C Ar); 156.5 (C-8a); 159.7 (C-7); 162.3 (C-2); 171.5 (C-4); 178.6 (C-5). Found, *m*/*z*: 280.1450 $[M+H]^+$. $C_{17}H_{18}N_3O$. Calculated, *m*/*z*: 280.1444.

7-Isopropyl-2-methyl-4-phenylpyrido[2,3-*d*]pyrimidin-5(8*H*)-one (3c). Pyrimidine **2c** (246 mg, 0.83 mmol) was added to a freshly prepared boiling solution of MeONa (89 mg, 1.65 mmol) in BuOH (7 ml). The mixture was refluxed for 1.5 h and cooled to room temperature, AcOH (0.4 ml) was added, and the mixture was stirred for 15 min. Reaction mixture was concentrated, the residue was suspended in MeOH (3 ml), and the precipitate (compound **3c**) was filtered off. The filtrate was concentrated, and the residue was dissolved in H_2O (30 ml) and extracted with $CHCl_3$ (3×10 ml). The combined organic layer was dried over Na_2SO_4 and concentrated. Obtained residue was washed with MeCN and dried to give compound **3c**. Yield 80 mg (35%), white solid, mp 240–241°C (MeCN), R_f 0.42 ($CHCl_3$–MeOH, 2:1). IR spectrum ($CHCl_3$), ν, cm^{-1}: 3408 (NH), 1640 (C=O), 1584, 1544, 1469. ^{1}H NMR spectrum (600 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 1.24 (6H, d, *J* = 6.9, $2CH_3$); 2.65 (3H, s, CH_3); 2.84–2.90 (1H, m, CH); 5.95 (1H, s, H-6); 7.35–7.39 (2H, m, H Ar); 7.40–7.44 (1H, m, H Ar); 7.46–7.49 (2H, m, H Ar); 12.11 (1H, br. s, NH). ^{13}C NMR spectrum (151 MHz, DMSO-d_6), δ, ppm: 21.0 ($2CH_3$); 25.6 (CH_3); 31.5 (CH); 109.6 (C-6); 110.9 (C-4a); 127.0 (2CH Ar); 128.8 (CH Ar); 129.3 (2CH Ar); 139.3 (C Ar); 156.9 (C-8a); 159.3 (C-7); 167.0 (C-2); 168.4 (C-4); 176.8 (C-5). Found, *m*/*z*: 280.1452 $[M+H]^+$. $C_{17}H_{18}N_3O$. Calculated, *m*/*z*: 280.1444.

4-Methyl-2-phenyl-7-(thiophen-2-yl)pyrido[2,3-*d*]-pyrimidin-5(8*H*)-one (3d). Pyrimidine **2d** (160 mg, 0.47 mmol) was added to a freshly prepared boiling solution of MeONa (38 mg, 0.71 mmol) in BuOH (5 ml). The mixture was refluxed for 30 min and cooled to room temperature. The precipitate was filtered off and suspended in H_2O (10 ml), AcOH (0.5 ml) was added, and the mixture was stirred for 15 min. The precipitate was filtered off and washed with H_2O. Yield 116 mg (77%), colorless solid, mp 235–236°C. IR spectrum ($CHCl_3$), ν, cm^{-1}: 3404 (NH), 1628 (C=O), 1603, 1592, 1580, 1564, 1540, 1492. ^{1}H NMR spectrum (600 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 3.16 (3H, s, CH_3); 6.63 (1H, s, H-6); 7.22 (1H, dd, *J* = 5.0, *J* = 3.7, H-4 Het); 7.50–7.55 (3H, m, CH Ar); 7.57 (1H, d, *J* = 5.0, H-5 Het); 7.60 (1H, d, *J* = 3.7, H-3 Het); 8.49–8.53 (2H, m, H Ar); 8.90 (1H, br. s, NH). ^{13}C NMR spectrum (151 MHz, $CDCl_3$), δ, ppm: 25.9 (CH_3); 111.9 (C-6); 113.6 (C-4a); 127.0 (3-CH Het); 128.6 (4-CH Het); 128.7 (2CH Ar); 128.9 (2CH Ar); 129.5 (5-CH Het); 131.6 (CH Ar); 135.4 (C-2 Het); 136.6 (C Ar); 142.6 (C-7); 156.3 (C-8a); 164.2

(C-2); 172.2 (C-4); 179.4 (C-5). Found, *m*/*z*: 320.0852 $[M+H]^+$. $C_{18}H_{14}N_3OS$. Calculated, *m*/*z*: 320.0852.

2,7-Dicyclopropyl-4-methylpyrido[2,3-*d*]pyrimidin-5(8*H*)-one (3e), mixture of two tautomers (pyridone **A**, hydroxypyridine **B**). Pyrimidine **2e** (42 mg, 0.16 mmol) was added to a freshly prepared boiling solution of MeONa (17 mg, 0.32 mmol) in BuOH (4 ml). The mixture was refluxed for 30 min and cooled to room temperature, AcOH (0.1 ml) was added, and the mixture was stirred for 15 min. The solution was concentrated, the residue was dissolved in H_2O (40 ml) and extracted with $CHCl_3$ (3×13 ml). The combined organic layer was dried over Na_2SO_4 and concentrated. The crude product was purified by column chromatography (SiO_2, $CHCl_3$; $CHCl_3$–MeOH, 100:1). Yield 12 mg (31%), colorless solid, mp 118–120°C, R_f 0.29 ($CHCl_3$–MeOH, 30:1). IR spectrum (KBr), ν, cm^{-1}: 3434, 3078, 2922 2854, 1649 (C=O), 1627, 1598, 1547, 1499, 1438, 1414, 1393, 1376, 1305, 1266, 1247, 1182, 1097, 1055, 1004, 954, 880, 821, 643, 538, 496. ^1H NMR spectrum (600 MHz, $CDCl_3$), δ, ppm: tautomer **A**: 0.94–0.98 (2H, m, CH_2); 1.12–1.20 (4H, m, $2CH_2$); 1.28–1.32 (1H, m, CH); 1.32–1.36 (2H, m, CH_2); 2.36–2.40 (1H, m, CH); 3.07 (3H, s, CH_3); 6.00 (1H, s, H-6); 8.80 (1H, br. s, NH); tautomer **B**: 0.94–0.98 (2H, m, CH_2); 1.12–1.20 (4H, m, $2CH_2$); 1.28–1.32 (1H, m, CH); 1.32–1.36 (2H, m, CH_2); 2.36–2.40 (1H, m, CH); 3.12 (3H, s, CH_3); 7.33 (1H, s, H-6); the signal of the OH group is not observed. ^{13}C NMR spectrum (151 MHz, $CDCl_3$), δ, ppm: tautomer **A**: 8.4 ($2CH_2$); 11.9 ($2CH_2$); 13.9 (CH); 17.6 (CH); 24.5 (CH_3); 110.6 (C-6); 112.7 (C-4a); 153.4 (C-8a); 155.6 (C-7); 171.3 (C-4); 171.6 (C-2); 179.1 (C-5); tautomer **B**: 8.4 ($2CH_2$); 11.0 ($2CH_2$); 12.2 (CH); 18.5 (CH); 28.0 (CH_3); 122.5 (C-6), signals of quaternary carbon atoms were not observed. Found, *m*/*z*: 242.1290 $[M+H]^+$. $C_{14}H_{16}N_3O$. Calculated, *m*/*z*: 242.1288.

***N*,*N*'-(5-Acetyl-6-methylpyrimidine-2,4-diyl)dipropanamide (6)**. A mixture of pyrimidine **5** (58 mg, 0.35 mmol) and propionic anhydride (0.36 ml, 2.80 mmol) in *o*-xylene (9 ml) was refluxed for 10 h, then cooled to room temperature. Solvent was evaporated, and the crude product was purified by column chromatography (SiO_2, $CHCl_3$; $CHCl_3$–MeOH, 60:1). Yield 40 mg (41%), colorless solid, mp 121–122°C (PhH–hexane), R_f 0.40 ($CHCl_3$–MeOH, 25:1). IR spectrum (KBr), ν, cm^{-1}: 3287 (NH), 3214 (NH), 3169 (NH), 3068, 2982, 2944, 1723 (C=O), 1699 (C=O), 1678 (C=O), 1599, 1565, 1514, 1393, 1368, 1252, 1174, 1078, 808, 772. ^1H NMR spectrum (600 MHz, DMSO-d_6), δ, ppm: 1.00–1.06 (6H, m, $C\underline{H}_3CH_2$); 2.29 (3H, s, CH_3CO); 2.39–2.45 (5H, s, CH_3, CH_2); 2.50–2.55 (2H, m, CH_2); 10.48 (1H, s, NH); 10.70 (1H, s, NH). ^{13}C NMR spectrum (151 MHz, DMSO-d_6), δ, ppm: 8.9 ($\underline{C}H_3CH_2$); 9.2 ($\underline{C}H_3CH_2$); 23.1 (CH_3); 28.9 ($CH_3\underline{C}H_2$); 29.7 ($CH_3\underline{C}H_2$); 30.0 ($\underline{C}H_3CO$); 119.7 (C-5); 154.9 (C-2); 156.4 (C-6); 166.2 (C-4); 172.6 (NCO); 173.6 (NCO); 197.9 (CO). Found, *m*/*z*: 279.1457 $[M+H]^+$. $C_{13}H_{19}N_4O_3$. Calculated, *m*/*z*: 279.1452.

2-Amino-7-ethyl-4-methylpyrido[2,3-*d*]pyrimidin-5(8*H*)-one (7). A solution of pyrimidine **6** (30 mg, 0.11 mmol) in BuOH (4 ml), heated to reflux, was added to solid MeONa (12 mg, 0.22 mmol). The mixture was refluxed for 30 min and then cooled to room temperature, AcOH (0.5 ml) was added, and the solution was concentrated. Then MeCN (20 ml) was added to the residue, the mixture was heated to reflux, and the precipitate was filtered off. The filtrate was concentrated, and the residue was purified by column chromatography (SiO_2, $CHCl_3$–MeOH, 60:1, 10:1). Yield 3.5 mg (16%), colorless solid, mp 247–250°C (MeCN), R_f 0.08 ($CHCl_3$–MeOH, 25:1). In addition, pyrimidine **5** was isolated (yield 10 mg (56%)). IR spectrum (KBr), ν, cm^{-1}: 3499 (NH), 3434 (NH), 3308 (NH), 3137, 2960, 2927, 2856, 1729 (C=O), 1649, 1603, 1547, 1512, 1464, 1401, 1286, 1126, 1074, 1041, 966, 861, 809, 744, 644, 545. ^1H NMR spectrum (600 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 1.15 (3H, t, *J* = 7.5, $C\underline{H}_3CH_2$); 2.44 (2H, q, *J* = 7.5, $CH_3C\underline{H}_2$); 2.69 (3H, s, CH_3); 7.51 (1H, s, H-6); 6.90 (2H, s, NH_2); 11.20 (1H, s, NH). ^{13}C NMR spectrum (151 MHz, DMSO-d_6), δ, ppm: 12.6 ($\underline{C}H_3CH_2$); 25.0 (CH_3); 25.5 (CH_2); 107.2 (C-4a); 109.8 (C-6); 153.6 (C-7); 157.8 (C-2); 161.9 (C-8a); 171.3 (C-4); 178.2 (C-5). Found, *m*/*z*: 205.1090 $[M+H]^+$. $C_{10}H_{13}N_4O$. Calculated, *m*/*z*: 205.1084.

***N*-[5-Acetyl-6-(methylsulfanyl)-2-phenylpyrimidin-4-yl]propanamide (8)**. A mixture of pyrimidine **1d** (96.8 mg, 0.37 mmol) and propionic anhydride (0.1 ml, 0.75 mmol) in PhMe (4 ml) was refluxed for 8 h, then cooled to room temperature. The precipitate was filtered off and washed with petroleum ether – 63 mg of compound **8** was obtained. Propionic anhydride (0.1 ml, 0.75 mmol) was added to the filtrate. The mixture was refluxed for 4 h, cooled to room temperature, and concentrated. The residue was washed with petroleum ether (5 ml) – 27 mg of compound **8** was obtained. Yield 90 mg (76%), white solid, mp 178–179°C (PhH–hexane). IR spectrum (KBr), ν, cm^{-1}: 3305 (NH), 3068, 2984, 2943, 2919, 1681 (C=O), 1565, 1508, 1481, 1386, 1356, 1280, 1247, 1194, 1073, 1027, 987, 941, 846, 807, 773, 697, 665. ^1H NMR spectrum (600 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 1.06 (3H, t, *J* = 7.5, $C\underline{H}_3CH_2$); 2.28 (3H, s, CH_3CO); 2.49 (2H, q, *J* = 7.5, $CH_3C\underline{H}_2$); 2.61 (3H, s, SCH_3); 7.53–7.60 (3H, m, H Ar); 8.41–8.46 (2H, m, H Ar); 11.00 (1H, s, NH). ^{13}C NMR spectrum (151 MHz, DMSO-d_6), δ, ppm: 8.9 ($\underline{C}H_3CH_2$); 13.7 (SCH_3); 28.9 ($\underline{C}H_3CO$); 29.0 (CH_2); 119.0 (C-5); 128.2 (2CH Ar); 128.7 (2CH Ar); 131.6 (CH Ar); 136.2 (C Ar); 153.6 (C-4); 161.5 (C-2); 169.1 (C-6); 173.9 (NCO); 196.2 (CO). Found, *m*/*z*: 316.1123 $[M+H]^+$. $C_{16}H_{18}N_3O_2S$. Calculated, *m*/*z*: 316.1114.

Synthesis of compounds 3f, 9, and 10a,b. *N*-[5-Acetyl-6-(methylsulfanyl)-2-phenylpyrimidin-4-yl]propanamide (**8**) (77 mg, 0.245 mmol) was added to a freshly prepared boiling solution of MeONa (26 mg, 0.49 mmol) in BuOH (4 ml). The mixture was refluxed for 1 h, then cooled to room temperature. The precipitate was filtered off and suspended in H_2O (10 ml), AcOH (0.2 ml) was added, and the mixture was stirred for 15 min. The precipitate was filtered off, washed with H_2O, and dried. Compound **3f** was obtained in a yield of 43 mg (58%). The BuOH solution (after the first filtration step) was concentrated, the residue was suspended in H_2O (10 ml), AcOH (0.2 ml) was added, and the mixture was stirred for 15 min. The precipitate was filtered off, washed with H_2O, dried. The residue was purified by column chromatography (SiO_2, $CHCl_3$; $CHCl_3$–

MeOH, 150:1). The reaction afforded compound **9** (11.2 mg, 16%) and a mixture of compounds **10a**,**b** (6.4 mg, 9%) in a **10a**/**10b** ratio of 5:1 (^{1}H NMR data).

7-Ethyl-4-(methylsulfanyl)-2-phenylpyrido[2,3-*d*]-pyrimidin-5(8*H*)-one (3f). Yield 43 mg (58%), colorless solid, mp 263–265°C (MeCN). IR spectrum (KBr), ν, cm^{-1}: 3236, 3177, 3133, 2961, 2921, 1730 (C=O), 1638, 1597, 1578, 1524, 1452, 1412, 1363, 1265, 1151, 1127, 1071, 1024, 994, 955, 867, 844, 779, 721, 694, 627, 551, 523. ^{1}H NMR spectrum (600 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 1.12 (3H, t, *J* = 6.7, C$\underline{H}_3$CH$_2$); 2.57 (3H, s, SCH$_3$); 2.60 (2H, q, *J* = 6.7, CH$_3$C$\underline{H}_2$); 6.06 (1H, s, H-6); 7.53–7.68 (3H, m, H Ar); 8.45–8.58 (2H, m, H Ar); 12.20 (1H, br. s, NH). ^{13}C NMR spectrum (151 MHz, DMSO-d_6), δ, ppm: 12.6 (C$\underline{H}_3$CH$_2$); 13.3 (SCH$_3$); 26.0 (CH$_2$); 111.0 (C-6); 111.7 (C-4a); 128.4 (2CH Ar); 128.7 (2CH Ar); 131.6 (CH Ar); 136.7 (C Ar); 155.4 (C-7); 155.6 (C-8a); 161.4 (C-2); 173.2 (C-4); 177.1 (C-5). Found, *m*/*z*: 298.1010 [M+H]$^+$. $C_{16}H_{16}N_3OS$. Calculated, *m*/*z*: 298.1009.

1-(4-Amino-6-butoxy-2-phenylpyrimidin-5-yl)ethan-1-one (9). Yield 11.2 mg (16%), colorless solid, mp 103–104°C (hexane). IR spectrum (KBr), ν, cm^{-1}: 3365 (NH), 2963, 2931, 2870, 1730 (C=O), 1632, 1609, 1561, 1525, 1449, 1426, 1365, 1344, 1282, 1253, 1134, 1068, 1025, 974, 952, 814, 785, 745, 710, 689, 577, 551. ^{1}H NMR spectrum (600 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 0.96 (3H, t, *J* = 7.4, C$\underline{H}_3$CH$_2$); 1.47–1.52 (2H, m, CH$_3$C$\underline{H}_2$); 1.78–1.82 (2H, m, CH$_2$); 2.55 (3H, s, CH$_3$CO); 4.56 (2H, t, *J* = 6.4, CH$_2$O); 7.51 (2H, t, *J* = 7.0, H Ar); 7.54 (1H, t, *J* = 7.0, H Ar); 7.92 (1H, br. s, NH); 8.34 (2H, d, *J* = 7.0, H Ar); 8.90 (1H, br. s, NH). ^{13}C NMR spectrum (151 MHz, DMSO-d_6), δ, ppm: 13.7 (C$\underline{H}_3$CH$_2$); 19.0 (CH$_2$); 30.5 (C$\underline{H}_3$CO); 33.4 (CH$_2$); 66.5 (CH$_2$O); 95.8 (C-5); 128.3 (2CH Ar); 128.4 (2CH Ar); 131.5 (CH Ar); 136.5 (C Ar); 163.3 (C-2); 164.8 (C-6); 169.3 (C-4); 197.9 (CO). Found, *m*/*z*: 286.1553 [M+H]$^+$. $C_{16}H_{20}N_3O_2$. Calculated, *m*/*z*: 286.1550.

A mixture of 5,6-dimethyl-4-(methylsulfanyl)-2-phenylpyrido[2,3-*d*]pyrimidin-7(8*H*)-one (10a) and 4-butoxy-5,6-dimethyl-2-phenylpyrido[2,3-*d*]pyrimidin-7(8*H*)-one (10b), ratio **10a**/**10b** = 5:1. Yield 6.4 mg (9%), colorless solid, mp 252–255°C.

Compound 10a. ^{1}H NMR spectrum (600 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 2.10 (3H, s, 6-CH$_3$); 2.68 (3H, s, 5-CH$_3$); 2.73 (3H, s, SCH$_3$); 7.52–7.58 (3H, m, H Ar); 8.44 (2H, d, *J* = 7.8, H Ar); 12.28 (1H, br. s, NH). ^{13}C NMR spectrum (151 MHz, DMSO-d_6), δ, ppm: 12.8 (CH$_3$); 14.5 (SCH$_3$); 19.8 (5-CH$_3$); 110.1 (C-4a); 128.1 (2CH Ar); 128.6 (C-6); 128.7 (2CH Ar); 131.3 (CH Ar); 136.4 (C Ar); 141.1 (C-5); 153.0 (C-8a); 158.8 (C-2); 162.1 (C-7); 167.7 (C-4). Found, *m*/*z*: 298.1006 [M+H]$^+$. $C_{16}H_{16}N_3OS$. Calculated, *m*/*z*: 298.1009.

Compound 10b. ^{1}H NMR spectrum (600 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 0.97 (3H, t, *J* = 7.4, C$\underline{H}_3$CH$_2$); 1.48–1.52 (2H, m, CH$_2$); 1.82–1.86 (2H, m, CH$_2$); 2.08 (3H, s, 6-CH$_3$); 2.55 (3H, s, 5-CH$_3$); 4.60 (2H, t, *J* = 6.4, CH$_2$O); 7.52–7.58 (3H, m, H Ar); 8.40 (2H, d, *J* = 7.8, H Ar); 12.28 (1H, br. s, NH). ^{13}C NMR spectrum (151 MHz, DMSO-d_6), δ, ppm: 12.4 (C$\underline{H}_3$CH$_2$); 13.8 (6-CH$_3$); 18.7 (CH$_2$); 19.0 (5-CH$_3$); 20.3 (CH$_2$); 66.9 (CH$_2$O); 128.0 (2CH Ar); 128.7 (2CH Ar); 128.8 (CH Ar); signals of quaternary carbon atoms are not observed.

2-(4-Chlorophenyl)-5-hydroxy-4,5-dimethyl-6-phenyl-5,8-dihydro[2,3-*d*]pyrimidin-7(6*H*)-one (11h) was detected after the storage of the solution of pyrimidine **2h** in DMSO-d_6 for 5 days. Compound **11h** was formed as a mixture of diastereomers, ratio of **A**/**B** diastereomers = 7:1. ^{1}H NMR spectrum (600 MHz, DMSO-d_6), δ, ppm (*J*, Hz): diastereomer **A**: 1.27 (3H, s, 5-CH$_3$); 2.70 (3H, s, 4-CH$_3$); 4.18 (1H, s, H-6); 5.60 (1H, s, OH); 7.23–7.73 (5H, m, H Ar); 7.60 (2H, d, *J* = 8.6, H Ar); 8.35 (2H, d, *J* = 8.6, H Ar); 11.10 (1H, br.s, NH); diastereomer **B**: 1.57 (3H, s, 5-CH$_3$); 2.67 (3H, s, 4-CH$_3$); 3.75 (1H, s, H-6); 5.46 (1H, s, OH); 7.23–7.37 (5H, m, H Ar); 7.60 (2H, d, *J* = 8.6, H Ar); 8.35 (2H, d, *J* = 8.6, H Ar); 11.22 (1H, br. s, NH). ^{13}C NMR spectrum (100 MHz, DMSO-d_6), δ, ppm: diastereomer **A**: 22.9 (5-CH$_3$); 24.4 (4-CH$_3$); 59.6 (C-6); 71.8 (C-5); 120.4 (C-4a); 126.9 (CH Ar); 127.3 (2CH Ar); 128.7 (2CH Ar); 129.3 (2CH Ar); 131.7 (2CH Ar); 133.9 (C Ar); 135.6 (C Ar); 156.2 (C-8a); 159.9 (C Ar); 164.4 (C-4); 170.3 (C-7); the signal of the C-2 atom apparently overlaps with the signal of another atom and can not be identified; diastereomer **B** (chemical shifts of some quaternary C atoms are given from the ^{1}H–^{13}C HMBC spectrum): 21.5 (5-CH$_3$); 24.3 (4-CH$_3$); 61.0 (C-6); 71.8 (C-5); 118.5 (C-4a); 126.9 (CH Ar); 127.3 (2CH Ar); 128.7 (2CH Ar); 129.3 (2CH Ar); 129.5 (2CH Ar); 135.5 (C Ar); 135.6 (C Ar); 164.8 (C-4); 171.0 (C-7); signals of other C atoms are not observed.

Synthesis of pyrido[2,3-*d*]pyrimidin-7(8*H*)-ones 4f–h (General method). Pyrimidine **2** (0.60 mmol) was added to a freshly prepared boiling solution of MeONa (65 mg, 1.20 mmol) in BuOH (4 ml). The mixture was refluxed for 40 min and cooled to room temperature followed by addition of AcOH (0.4 ml). The obtained precipitate was filtered off and washed with H_2O (in the case of compounds **4f**,**h**). In the case of compound **4g**, BuOH was removed under reduced pressure and residue was sequentially washed with H_2O (15 ml) and PhH (15 ml).

4,5-Dimethyl-2,6-diphenylpyrido[2,3-*d*]pyrimidin-7(8*H*)-one (4f). Yield 100 mg (51%), pale-yellow solid, mp 257–258°C (BuOH). IR spectrum ($CHCl_3$), ν, cm^{-1}: 3384 (NH), 1664 (C=O), 1592, 1584, 1528. ^{1}H NMR spectrum (500 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 2.40 (3H, s, 5-CH$_3$); 2.97 (3H, s, 4-CH$_3$); 7.25 (2H, d, *J* = 7.2, H Ar); 7.39 (1H, t, *J* = 7.2, H Ar); 7.46 (2H, t, *J* = 7.2, H Ar); 7.54–7.58 (3H, m, H Ar); 8.43–8.48 (2H, m, H Ar); 12.35 (1H, s, NH). Found, *m*/*z*: 328.1437 [M+H]$^+$. $C_{21}H_{18}N_3O$. Calculated, *m*/*z*: 328.1444.

2,5-Dimethyl-4,6-diphenylpyrido[2,3-*d*]pyrimidin-7(8*H*)-one (4g). Yield 94 mg (48%), pale-yellow solid, mp 225–226°C (MeCN). IR spectrum (KBr), ν, cm^{-1}: 3060, 2978, 2914, 1655 (C=O), 1584, 1525, 1495, 1477, 1435, 1423, 1378, 1360, 1331, 1243, 1076, 1036, 978, 888, 772, 752, 705, 681, 645, 573, 538. ^{1}H NMR spectrum (600 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 1.67 (3H, s, 5-CH$_3$); 2.82 (3H, s, 2-CH$_3$); 7.24 (2H, d, *J* = 7.4, H Ar); 7.36 (1H, t, *J* = 7.4, H Ar); 7.43 (2H, t, *J* = 7.4, H Ar); 7.46–7.52 (5H, m, CH Ar); 9.97 (1H, s, NH). ^{13}C NMR spectrum (151 MHz, $CDCl_3$), δ, ppm: 22.1 (CH$_3$); 25.8 (CH$_3$); 110.4 (C-4a); 128.1 (CH Ar);

128.4 (2CH Ar); 128.5 (2CH Ar); 128.6 (2CH Ar); 129.6 (CH Ar); 129.9 (2CH Ar); 135.0 (C Ar); 135.6 (C-6); 140.4 (C Ar); 143.9 (C-5); 154.3 (C-8a); 161.9 (C-7); 166.3 (C-2); 166.6 (C-4). Found, *m*/*z*: 328.1434 $[M+H]^+$. $C_{21}H_{18}N_3O$. Calculated, *m*/*z*: 328.1444.

2-(4-Chlorophenyl)-4,5-dimethyl-6-phenylpyrido[2,3-*d*]-pyrimidin-7(8*H*)-one (4h). Yield 140 mg (65%), pale-yellow solid, mp 283–285°C (EtOH). IR spectrum (KBr), ν, cm^{-1}: 3065, 2981, 2928, 1648 (C=O), 1565, 1524, 1422, 1379, 1355, 1286, 1245, 1170, 1085, 1010, 915, 847, 807, 756, 707, 624, 567, 540, 484. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 2.40 (3H, s, 5-CH_3); 2.96 (3H, s, 4-CH_3); 7.24 (2H, d, *J* = 7.2, H Ar); 7.38 (1H, t, *J* = 7.2, H Ar); 7.45 (2H, t, *J* = 7.2, H Ar); 7.61 (2H, d, *J* = 8.5, CH Ar); 8.43 (2H, d, *J* = 8.5, CH Ar); 12.30 (1H, s, NH). ^{13}C NMR spectrum (100 MHz, DMSO-d_6), δ, ppm: 21.5 (CH_3); 27.6 (CH_3); 111.6 (C-4a); 127.5 (CH Ar); 128.1 (2CH Ar); 128.7 (2CH Ar); 129.7 (2CH Ar); 130.1 (2CH Ar); 134.6 (C-6); 135.3 (C Ar); 136.0 (C Ar); 136.1 (C Ar); 143.3 (C-5); 154.6 (C-8a); 159.6 (C-2); 161.6 (C-7); 166.2 (C-4). Found, *m*/*z*: 362.1038 $[M+H]^+$. $C_{21}H_{17}ClN_3O$. Calculated, *m*/*z*: 362.1055.

Synthesis of pyrido[2,3-*d*]pyrimidin-7(8*H*)-ones 4i,j (General method). A mixture of pyrimidine **2f**,**h** (0.30 mmol) and DMF–DMA (80 μl, 0.6 mmol) in PhH (5 ml) was refluxed for 5 h and then cooled to room temperature. The volatile components were evaporated. The residue was washed with petroleum ether (15 ml) and suspended in MeCN (5 ml). The precipitate was filtered off. The filtrate was concentrated to give products **4i**,**j**.

4,5,8-Trimethyl-2,6-diphenylpyrido[2,3-*d*]pyrimidin-7(8*H*)-one (4i). Yield 68 mg (66%), pale-yellow solid, mp 208–210°C (PhH–hexane). IR spectrum (KBr), ν, cm^{-1}: 1643 (C=O), 1584, 1542, 1461, 1424, 1378, 1332, 1283, 1247, 1204, 1104, 1062, 989, 792, 767, 701, 657, 607, 570, 520. ^{1}H NMR spectrum (600 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 2.40 (3H, s, 5-CH_3); 2.99 (3H, s, 4-CH_3); 3.78 (3H, s, 8-CH_3); 7.25 (2H, d, *J* = 7.2, H Ar); 7.40 (1H, t, *J* = 7.2, H Ar); 7.46 (2H, t, *J* = 7.2, H Ar); 7.55–7.61 (3H, m, CH Ar); 8.48–8.54 (2H, m, CH Ar). ^{13}C NMR spectrum (151 MHz, DMSO-d_6), δ, ppm: 21.5 (5-CH_3); 27.9 (4-CH_3); 28.7 (8-CH_3); 112.2 (C-4a); 127.5 (CH Ar); 128.1 (4CH Ar); 128.7 (2CH Ar); 130.0 (2CH Ar); 131.3 (CH Ar); 133.5 (C-6); 136.4 (2C Ar); 142.0 (C-5); 154.3 (C-8a); 159.9 (C-2); 161.2 (C-7); 166.3 (C-4). Found, *m*/*z*: 342.1587 $[M+H]^+$. $C_{22}H_{20}N_3O$. Calculated, *m*/*z*: 342.1601.

2-(4-Chlorophenyl)-4,5,8-trimethyl-6-phenylpyrido-[2,3-*d*]pyrimidin-7(8*H*)-one (4j). Yield 70 mg (62%), pale-yellow solid, mp 174–175°C (PhH–hexane). IR spectrum (KBr), ν, cm^{-1}: 3065, 2981, 2918, 1648 (C=O), 1565, 1524, 1422, 1335, 1286, 1245, 1170, 1085, 1010, 915, 847, 807, 756, 707, 624, 567, 540, 484. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 2.38 (3H, s, 5-CH_3); 2.94 (3H, s, 4-CH_3); 3.73 (3H, s, 8-CH_3); 7.24 (2H, d, *J* = 7.0, H Ar); 7.40 (1H, t, *J* = 7.0, H Ar); 7.47 (2H, t, *J* = 7.0, H Ar); 7.60 (2H, d, *J* = 8.6, H Ar); 8.45 (2H, d, *J* = 8.6, H Ar). ^{13}C NMR spectrum (101 MHz, DMSO-d_6), δ, ppm: 21.6 (5-CH_3); 27.9 (4-CH_3); 28.7 (8-CH_3); 112.3 (C-4a); 127.6 (CH Ar); 128.1 (2CH Ar); 128.8 (2CH Ar); 129.8 (2CH Ar); 130.0 (2CH Ar); 133.6 (C-6); 135.2 (C Ar); 136.2 (C Ar); 136.3 (C Ar); 142.0 (C-5); 154.2 (C-8a); 158.7 (C-2); 161.2 (C-7); 166.4 (C-4). Found, *m*/*z*: 376.1204 $[M+H]^+$. $C_{22}H_{19}ClN_3O$. Calculated, *m*/*z*: 376.1211.

4,8-Dimethyl-2-phenylpyrido[2,3-*d*]pyrimidin-5(8*H*)-one (12). A mixture of pyrimidine **2a** (100 mg, 0.35 mmol) and DMF–DMA (0.10 ml, 0.75 mmol) in PhH (5 ml) was refluxed for 3 h and then cooled to room temperature. The volatile components were evaporated, and the residue was purified by column chromatography (SiO_2, $CHCl_3$; $CHCl_3$–MeOH, 60:1). Yield 48 mg (55%), colorless solid, mp 206–208°C, R_f 0.64 ($CHCl_3$–MeOH, 25:1). IR spectrum (KBr), ν, cm^{-1}: 3065, 2942, 1634 (C=O), 1597, 1555, 1491, 1362, 1259, 1183, 1167, 1071, 834, 724, 694, 552, 460. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 2.97 (3H, s, 4-CH_3); 3.83 (3H, s, 8-CH_3); 6.18 (1H, d, *J* = 7.9, H-6); 7.52–7.60 (3H, m, CH Ar); 8.04 (1H, d, *J* = 7.9, H-7); 8.48–8.52 (2H, m, CH Ar). ^{13}C NMR spectrum (101 MHz, DMSO-d_6), δ, ppm: 25.8 (4-CH_3); 37.6 (8-CH_3); 114.1 (C-6); 114.6 (C-4a); 128.5 (2CH Ar); 128.7 (2CH Ar); 131.6 (CH Ar); 136.3 (C Ar); 144.5 (C-7); 155.4 (C-8a); 161.7 (C-2); 171.1 (C-4); 178.0 (C-5). Found, *m*/*z*: 252.1127 $[M+H]^+$. $C_{15}H_{14}N_3O$. Calculated, *m*/*z*: 252.1131.

(*E*)-4-[2-(Dimethylamino)vinyl]-8-methyl-2-phenylpyrido-[2,3-*d*]pyrimidin-5(8*H*)-one (13) was obtained as a byproduct during chromatographic separation of compound **12**. Yield 22 mg (21%), yellow solid, mp 192–194°C, R_f 0.36 ($CHCl_3$–MeOH, 25:1). IR spectrum (KBr), ν, cm^{-1}: 3059, 2938, 1641 (C=O), 1606, 1527, 1487, 1424, 1370, 1254, 1209, 1107, 1049, 970, 842, 720, 690, 467. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 2.99 (3H, s, NCH_3); 3.22 (3H, s, NCH_3); 3.75 (3H, s, 8-CH_3); 6.00 (1H, d, *J* = 7.8, H-6); 7.41 (1H, d, *J* = 12.5, H vinyl); 7.45–7.50 (3H, m, H Ar); 7.81 (1H, d, *J* = 7.8, H-7); 8.48–8.50 (2H, m, H Ar); 8.52 (1H, d, *J* = 12.5, H vinyl). ^{13}C NMR spectrum (101 MHz, DMSO-d_6), δ, ppm: 37.3 (NCH_3); 37.6 (8-CH_3); 44.8 (NCH_3); 93.7 (CH vinyl); 108.3 (C-4a); 113.8 (C-6); 128.3 (4CH Ar); 130.7 (CH Ar); 137.7 (C Ar); 142.6 (C-7); 152.7 (CH vinyl); 156.4 (C-8a); 160.4 (C-2); 165.7 (C-4); 178.5 (C-5). Found, *m*/*z*: 307.1553 $[M+H]^+$. $C_{18}H_{19}N_4O$. Calculated, *m*/*z*: 307.1553.

Synthesis of pyrimido[4,5-*d*][1,3]oxazines 14a,b (General method). A mixture of pyrimidine **1a** (0.18 g, 0.80 mmol) and acyl chloride (1.60 mmol) in *o*-xylene (5 ml) was refluxed for 6 h, and Et_3N (0.33 ml, 2.40 mmol) was added. The mixture was refluxed for 2 h and then cooled to room temperature. The precipitate was filtered off, and the filtrate was concentrated. The crude product was purified by column chromatography (SiO_2, PhH; PhH–$CHCl_3$, 1:1).

5-Methyl-4-methylidene-7-phenyl-2-(thiophen-2-yl)-4*H*-pyrimido[4,5-*d*][1,3]oxazine (14a). Yield 107 mg (42%), yellow solid, mp 189–190°C (PhH–hexane), R_f 0.56 (PhH–EtOH, 40:1). IR spectrum (KBr), ν, cm^{-1}: 1628, 1596, 1544, 1528, 1428, 1408, 1352, 1240, 1152, 1116, 1024, 980, 892, 852, 824, 788, 728, 700. ^{1}H NMR spectrum (600 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 2.75 (3H, s, CH_3); 4.91 (1H, d, *J* = 3.2, CH_2); 5.21 (1H, d, *J* = 3.2, CH_2); 7.19 (1H, dd, *J* = 4.8, *J* = 3.4, H-4 Het); 7.46–7.52 (3H, m, H Ar); 7.68 (1H, d, *J* = 4.8, H-5 Het); 8.03 (1H, d, *J* = 3.4, H-3 Het);

8.52–8.58 (2H, m, H Ar). ^{13}C NMR spectrum (151 MHz, $CDCl_3$), δ, ppm: 25.6 (CH_3); 96.6 (CH_2); 110.8 (C-4a); 128.2 (CH-4 Het); 128.4 (2CH Ar); 128.7 (2CH Ar); 131.0 (CH Ar); 133.1 (CH-3 Het); 133.6 (CH-5 Het); 134.9 (C-2 Het); 136.8 (C Ar); 148.9 (C-4); 159.6 (C-2); 159.6 (C-8a); 163.8 (C-5); 164.5 (C-7). Found, *m*/*z*: 320.0846 $[M+H]^+$. $C_{18}H_{14}N_3OS$. Calculated, *m*/*z*: 320.0852.

5-Methyl-4-methylidene-2,7-diphenyl-4*H*-pyrimido-[4,5-*d*][1,3]oxazine (14b). Yield 90 mg (36%), yellow solid, mp 175–176°C (PhH–hexane), R_f 0.50 ($CHCl_3$). IR spectrum (KBr), ν, cm^{-1}: 1636, 1612, 1580, 1548, 1528, 1452, 1412, 1352, 1304, 1232, 1176, 1160, 1116, 1068, 1024, 980, 896, 824, 780, 696. ^{1}H NMR spectrum (600 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 2.76 (3H, s, CH_3); 4.94 (1H, d, *J* = 2.9, CH_2); 5.23 (1H, d, *J* = 2.9, CH_2); 7.46–7.56 (5H, m, H Ar); 7.61 (1H, t, *J* = 7.7, H Ar); 8.33 (2H, d, *J* = 7.7, H Ar); 8.52–8.60 (2H, m, H Ar). ^{13}C NMR spectrum (151 MHz, $CDCl_3$), δ, ppm: 25.6 (CH_3); 96.4 (CH_2); 111.0 (C-4a); 128.4 (2CH Ar); 128.5 (2CH Ar); 128.7 (2CH Ar); 129.0 (2CH Ar); 129.9 (C Ar); 131.0 (CH Ar); 133.3 (CH Ar); 136.8 (C Ar); 149.1 (C-4); 159.6 (C-8a); 163.4 (C-2); 164.0 (C-5); 164.5 (C-7). Found, *m*/*z*: 314.1289 $[M+H]^+$. $C_{20}H_{16}N_3O$. Calculated, *m*/*z*: 314.1288.

Rearrangement of 5-methyl-4-methylidene-7-phenyl-2-(thiophen-2-yl)-4*H*-pyrimido[4,5-*d*][1,3]oxazine (14a) to 4-methyl-2-phenyl-7-(thiophen-2-yl)pyrido[2,3-*d*]pyrimidin-5(8*H*)-one (3d). Compound **14a** (50 mg, 0.16 mmol) was added to a freshly prepared boiling solution of MeONa (17 mg, 0.31 mmol) in BuOH (7 ml). The mixture was refluxed for 30 min. The reaction was accompanied by the decoloration of the solution. The mixture was cooled to room temperature. The precipitate was filtered off and washed with H_2O (10 ml). AcOH (0.2 ml) was added, and the mixture was refluxed for 10 min. The precipitate was filtered off and washed with H_2O. Yield 34 mg (68%). The spectral data and mp are identical to the characteristics of compound **3d** prepared by the above-described procedure.

X-ray structural analysis of compounds 3a and 4i was performed at 100K on a Bruker Quest D8 diffractometer equipped with a Photon-III area detector (shutterless φ- and ω-scan technique) using graphite-monochromatized MoKα radiation (λ 0.71073 Å). The intensity data were integrated by the SAINT program[42] and corrected for absorption and decay using SADABS.[43] The structures were solved by direct methods using SHELXT and refined on F^2 using SHELXL-2018.[44] The structures were deposited at the Cambridge Crystallographic Data Center (deposits CCDC 2051962 and CCDC 2051963).

Supplementary information file containing NMR data of all synthesized compounds and results of X-ray crystallographic analysis for compounds **3a** and **4i** is available at the journal website at http://link.springer.com/journal/10593.

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