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One-Pot Synthesis of Thieno[2,3-*b*]pyridine and Pyrido[3′,2′:4,5]thieno[3,2-*d*]pyrimidine Derivatives

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Abstract—2-Acyl-4,5,6-trialkyl-3-aminothieno[2,3-*b*]pyridines, 8′-ethyl-7′,9′-dimethyl-1′*H*-spiro[cyclohexane-1,2′-pyrido[3′,2′:4,5]thieno[3,2-*d*]pyrimidin]-4′(3′*H*)-one, and 7,8,9-trimethylpyrido[3′,2′:4,5]thieno[3,2-*d*]pyrimidin-4-amine have been synthesized by one-pot three-component condensation of 3-methyl(ethyl)pentane-2,4-diones with cyanothioacetamide and α-halocarbonyl compounds, cyclohexanone, or formamide. The structures of some of the synthesized thieno[2,3-*b*]pyridine derivatives have been studied by X-ray analysis.

Keywords: 3-methyl(ethyl)pentane-2,4-diones, cyanothioacetamide, α-halocarbonyl compounds, cyclohexanone, formamide, thieno[2,3-*b*]pyridines, pyrido[3′,2′:4,5]thieno[3,2-*d*]pyrimidines, X-ray analysis

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Functionalized thieno[2,3-*b*]pyridines are used in the treatment of central nervous system diseases [1] and as C-terminal hydrolase L1 (UCH-L1) inhibitors [2]. They are also promising for the design of antimicrobial [3] and antitumor agents [4–6]. The main methods of synthesis of these compounds are based on fusion of a thiophene ring to pyridine or a pyridine ring to thiophene [7].

Herein, we report a one-pot procedure for the synthesis of 2-acyl-4,5,6-trialkyl-3-aminothieno[2,3-*b*]-pyridines **1a**–**1l** that are promising as starting materials for the preparation of fused polycyclic heterocycles [8–11]. Compounds **1a**–**1l** were obtained by condensation of acyclic precursors, pentane-2,4-diones **2a**–**2c**, cyanothioacetamide (**3**), and α-halo ketones **4a**–**4l**, in DMF at 50°C in the presence of an equimolar amount of sodium ethoxide. A plausible reaction scheme includes Knoevenagel condensation of cyanothioacetamide at one carbonyl group of diketone **2**, intramolecular cyclization of condensation product **A** to sodium pyridine-2-thiolate **B**, and alkylation of the latter with α-halocarbonyl compound **4** with the formation of organic sulfides **C** that are capable of undergoing deprotonation in basic medium to give carbanion **D**. Intramolecular cyclization with participation of the cyano group leads to imino derivative **E** which tautomerizes to exhaustively substituted 3-aminothieno-[2,3-*b*]pyridine **1** (Scheme 1).

The structures of (3-amino-4,6-dimethylthieno-[2,3-*b*]pyridin-2-yl)(thiophen-2-yl)methanone (**1a**),

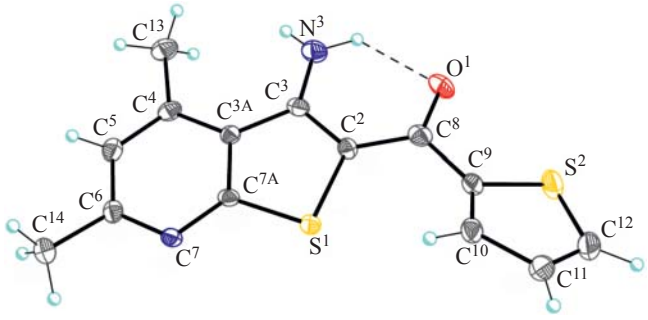
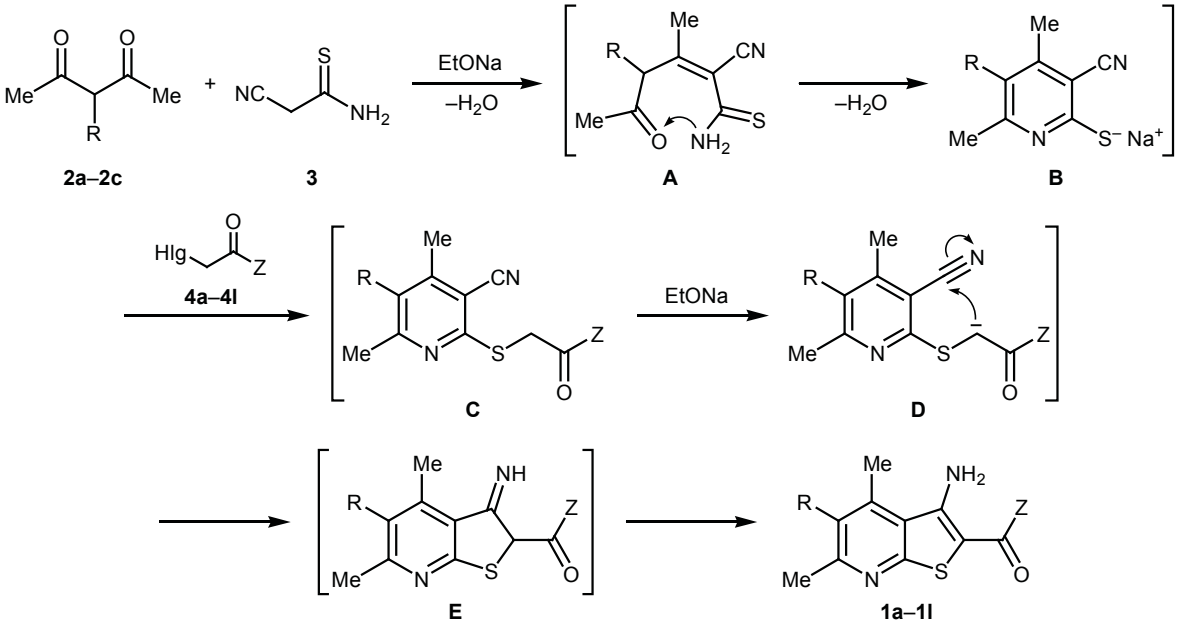


Fig. 1. Molecular structure of compound **1a**. Non-hydrogen atoms are shown as 50%-probability anisotropic displacement ellipsoids. Intramolecular hydrogen bond N–H···O is shown with dashed line.

Scheme 1.



1, R = H, Z = thiophen-2-yl (**a**), 4-ClC_6H_4 (**b**), 4-$MeOC_6H_4$ (**c**), BuO (**d**), 1,3-thiazol-2-ylamino (**e**), *i*-PrO (**f**), PrO (**g**), 4-AcC_6H_4NH (**h**), $Me(CH_2)_7O$ (**i**); R = Me, Z = 2-MeC_6H_4NH (**j**); R = Et, PhNH (**k**), 4-BrC_6H_4 (**l**). **2**, R = H (**a**), Me (**b**), Et (**c**); **4**, Hlg = Br, Z = thiophen-2-yl (**a**), 4-ClC_6H_4 (**b**), 4-$MeOC_6H_4$ (**c**), 4-BrC_6H_4 (**l**); Hlg = Cl, Z = BuO (**d**), 1,3-thiazol-2-ylamino (**e**), *i*-PrO (**f**), PrO (**g**), 4-AcC_6H_4NH (**h**), $Me(CH_2)_7O$ (**i**), 2-MeC_6H_4NH (**j**), PhNH (**k**).

(3-amino-4,6-dimethylthieno[2,3-*b*]pyridin-2-yl)-(4-chlorophenyl)methanone (**1b**), and (3-amino-4,6-dimethylthieno[2,3-*b*]pyridin-2-yl)(4-methoxyphenyl)-methanone (**1c**) were studied by X-ray analysis. The central 3-amino-4,6-dimethylthieno[2,3-*b*]pyridin-2-yl)carbonyl fragment of all molecules **1a**–**1c** is almost planar [mean-square deviation of non-hydrogen atoms from the average plane are 0.039 (**1a**), 0.055 (**1b**), and 0.045 Å (**1c**)]. Presumably, the planar structure of that fragment is stabilized by the formation of extended conjugation system and fairly strong intramolecular hydrogen bond N–H···O (Figs. 1–3, Table 1).

The planar thienyl (**1a**), *p*-chlorophenyl (**1b**), and *p*-methoxyphenyl (**1c**) groups are turned through angles of 28.38(10), 33.00(5), and 37.09(4)°, respectively, relative to the 3-amino-4,6-dimethylthieno-[2,3-*b*]pyridin-2-ylcarbonyl fragment. It should be noted that the methoxy group in molecule **1c** is co-

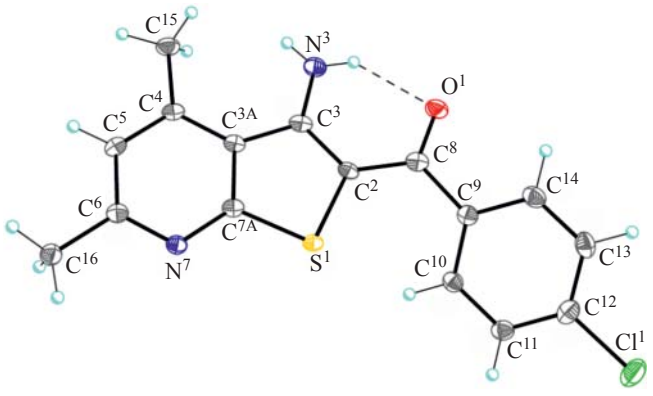


Fig. 2. Molecular structure of compound **1b**. Non-hydrogen atoms are shown as 50%-probability anisotropic displacement ellipsoids. Intramolecular hydrogen bond N–H···O is shown with dashed line.

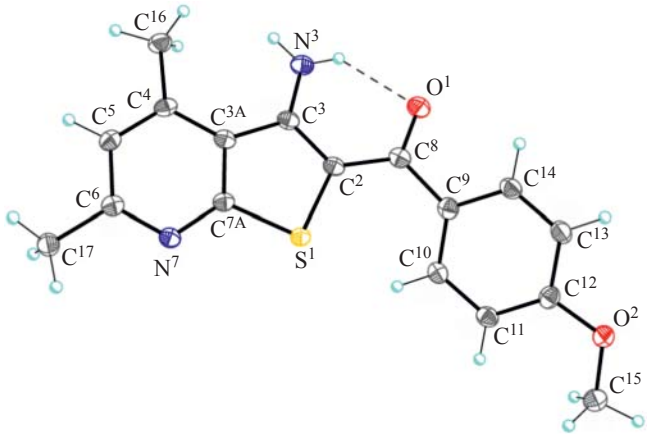


Fig. 3. Molecular structure of compound **1c**. Non-hydrogen atoms are shown as 50%-probability anisotropic displacement ellipsoids. Intramolecular hydrogen bond N–H···O is shown with dashed line.

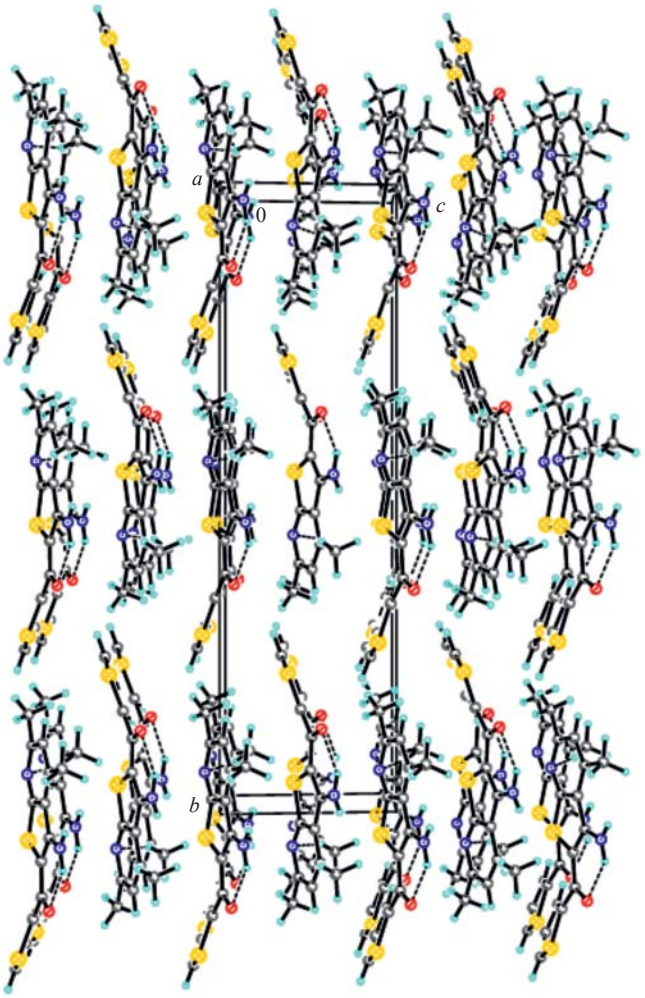


Fig. 4. Crystal packing of compound **1a**.

planar to the benzene ring. Molecules **1a**, **1b**, and **1c** in crystal are packed in stacks along the *a* crystallographic axis (Figs. 4–6). The stacked molecules are oriented approximately parallel to the (1 0 –2) plane. No short intermolecular contacts were observed in the crystal structures of **1a**–**1c**.

It should be noted that compounds **1b** and **1c** are isostructural and that compound **1a** is isotypical to **1b** and **1c**. Obviously, this is related to the different mutual arrangement of stacks. In the crystal structure of **1a**, the stacks are aligned along the *b* crystallographic axis in a "head-to-tail" fashion with conservation of the polar direction (polar space group *Cc*), whereas the crystal structures of **1b** and **1c** are characterized by head-to-head orientation of stacks along the same direction, so that an inversion center appears (centrosymmetric space group $P2_1/c$). Therefore, compounds **1a**–**1c** can be expected to form the corresponding polymorphic modifications, namely, in the centrosymmetric space group $P2_1/c$ for **1a** and polar space group *Cc* for **1b** and **1c**.

The condensation of 3-methylpentane-2,4-dione (**2b**) with cyanothioacetamide (**3**) in DMF in the presence of sodium ethoxide at 50°C, followed by addition of chloroacetonitrile (**5**) and heating of the product in boiling formamide for 1 h, afforded 7,8,9-trimethylpyrido[3′,2′:4,5]thieno[3,2-*d*]pyrimidin-4-amine (**6**). Thienopyridine **F** was obviously formed as intermediate product in this multicomponent process (Scheme 2). Likewise, the condensation of 3-ethylpentane-2,4-dione (**2c**), cyanothioacetamide (**3**), chloroacetamide (**7**), and cyclohexanone under similar conditions led to the formation of 8′-ethyl-7′,9′-dimethyl-1′*H*-spiro[cyclohexane-1,2′-pyrido[3′,2′:4,5]-thieno[3,2-*d*]pyrimidin]-4′(3′*H*)-one (**8**) which is a potential intermediate product in the synthesis of antimicrobial [12], anti-asthmatic [13], and analgesic agents [14]. It is reasonable to presume intermediate formation of substituted thienopyridine **G** in this reaction (Scheme 2).

The spectral parameters of **1a**–**1l**, **6**, and **8** were consistent with their structures (see Experimental). Their ^{1}H NMR spectra showed signals from aliphatic substituents at proper positions with expected multiplicities, as well as broadened singlets of NH and NH_2 protons. The formation of spirocyclic fragment in **8** confirmed vicinal position of the amino and carbamoyl groups, which is typical of such systems [15].

EXPERIMENTAL

The unit cell parameters and reflections intensities for compounds **1a**–**1c** were measured on a BELOK synchrotron station at the Kurchatov Institute National

Table 1. Hydrogen bonds in the crysatal structures of compounds **1a**–**1c**

Compound no.	D–H···A, Å	*d*(D–H), Å	*d*(H···A), Å	*d*(D···A), Å	Angle DHA, deg
1a	N^3–H^{3A}···O^1	0.90(5)	2.01(5)	2.712(5)	133(4)
1b	N^3–H^{3A}···O^1	0.85(2)	2.04(2)	2.697(2)	133.6(19)
1c	N^3–H^{3A}···O^1	0.84(2)	2.08(2)	2.693(2)	129.7(17)

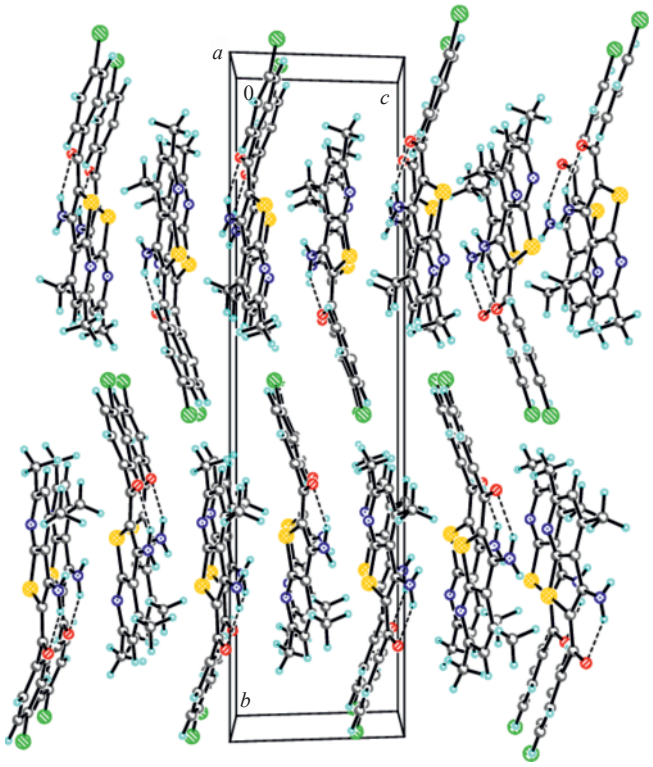


Fig. 5. Crystal packing of compound **1b**.

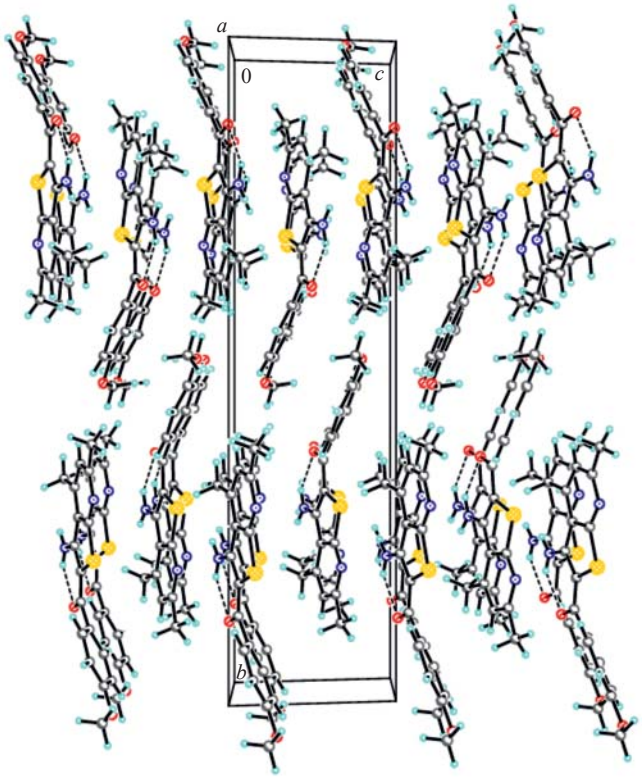


Fig. 6. Crystal packing of compound **1c**.

Research Center using a Rayonix SX165 CCD two-coordinate detector (temperature 100 K, λ 0.96990 Å, φ-scanning with a step of 1.0°). The data were processed by iMOSFLM program included in CCP4 package [16]. A correction for absorption of X-rays was applied using SCALA program [17]. The principal crystallographic data and structure refinement parameters are collected in Table 2. The structures were solved by the direct method and were refined against F^2 by the full-matrix least squares method in anisotropic approximation for non-hydrogen atoms. Hydrogen atoms of the amino groups were localized by the difference Fourier syntheses and were refined in isotropic approximation with fixed thermal displacement parameters [U_{iso}(H) = 1.2U_{eq}(N)]. The positions of the other hydrogen atoms for all compounds were calculated geometrically and were refined according to the riding model with fixed positional parameters and isotropic thermal displacement parameters [U_{iso}(H) = 1.5U_{eq}(C) for methyl groups U_{iso}(H) = 1.2U_{eq}(C) for other hydrogens]. All calculations were performed using SHELXTL software package [18]. The tabulated

Scheme 2.

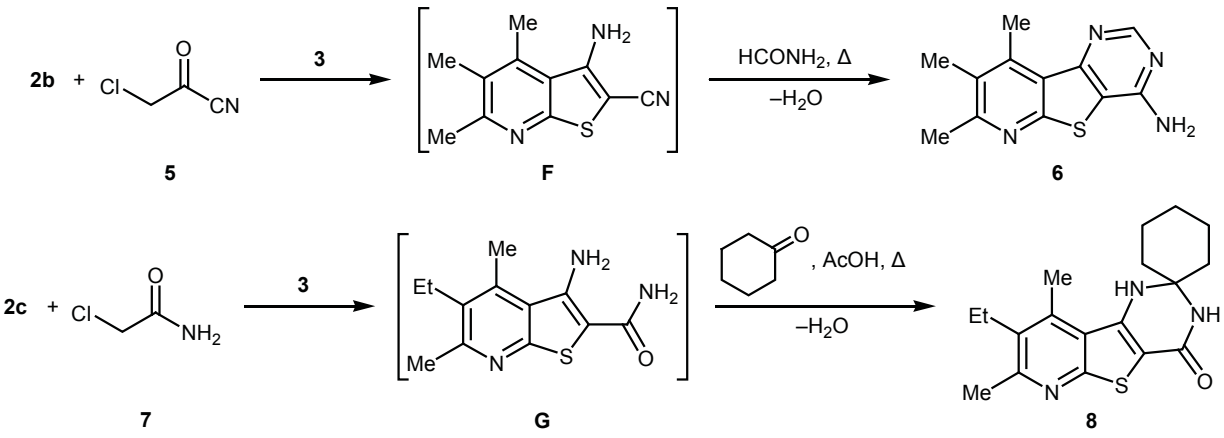


Table 2. Crystallographic data for compounds **1a–1c**

Parameter	**1a**	**1b**	**1c**
Formula	$C_{14}H_{12}N_2OS_2$	$C_{16}H_{13}ClN_2OS$	$C_{17}H_{16}N_2O_2S$
Molecular weight	288.38	316.79	312.38
Single crystal dimensions, mm	0.05×0.15×0.25	0.10×0.10×0.25	0.10×0.10×0.20
Crystal system	Monoclinic	Monoclinic	Monoclinic
Space group	*Cc*	$P2_1/c$	$P2_1/c$
a, Å	6.9652(14)	7.1131(14)	7.1300(14)
b, Å	25.630(5)	27.840(6)	28.265(6)
c, Å	7.2852(15)	7.2401(14)	7.2850(15)
β, deg	97.37(3)	100.67(3)	100.89(3)
V, Å^3	1289.8(5)	1409.0(5)	1441.7(5)
Z	4	4	4
d_{calc}, g/cm^3	1.485	1.493	1.439
F(000)	600	656	656
μ	0.956	0.988	0.537
2θ	76.76	76.86	76.98
Total number of reflections	6331	18340	25378
Number of independent reflections (R_{int})	2054 (0.054)	3017 (0.104)	2995 (0.070)
Number of reflections with $I > 2\sigma(I)$	1947	2548	2645
Number of variables	181	199	209
R_1; wR_2 [reflections $I > 2\sigma(I)$]	0.041; 0.090	0.048; 0.123	0.039; 0.097
R_1; wR_2 (all independent reflections)	0.048; 0.097	0.057; 0.130	0.046; 0.102
Goodness of fit with respect to F^2	1.046	1.080	1.055
Extinction coefficient	0.004(1)	0.013(2)	0.006(1)
T_{min}; T_{max}	0.770; 0.940	0.770; 0.900	0.770; 0.900

coordinates of atoms, bond lengths, bond and torsion angles, and anisotropic displacement parameters for compounds **1a**–**1c** were deposited to the Cambridge Crystallographic Data Centre [entry nos. 1 880 558 (**1a**), 1 880 559 (**1b**), and 1 880 560 (**1c**)].

The IR spectra were recorded on an IKS-40 spectrometer from samples dispersed in mineral oil. The ^{1}H and ^{13}C NMR spectra were measured on a Varian VXR–400 spectrometer at 399.97 and 100 MHz, respectively, using DMSO-d_6 as solvent (unless otherwise stated) and tetramethylsilane as internal standard. The mass spectra of **1a**–**1c**, **1e**, **1f**, **1h**, **1i**, and **6** were obtained on an Orbitrap Elite high-resolution mass spectrometer; samples were dissolved in 1 mL of DMSO, and the solutions were diluted 100-fold with 1% HCOOH in CH_3CN and introduced into the electrospray ionization source at a flow rate of 40 μL/min using a syringe pump; ion source gas supply was turned off; capillary voltage 3.5 kV, capillary temperature 275°C; positive and negative ion detection, Orbitrap resolution 480 000; internal calibrants $[2DMSO + H]^+$ ion (*m*/*z* 157.03515) for positive ions and dodecyl sulfate anion (*m*/*z* 265.14789) for negative ions. The mass spectra of **1d**, **1g**, **1j**–**1l**, and **8** (electron impact, 70 eV) were recorded using an Agilent 1100 Series liquid chromatograph coupled with an Agilent LC/MSD LS mass-selective detector (samples were introduced in acetic acid). Elemental analysis was performed with a Perkin Elmer CHN analyzer. The melting points were measured on a Kofler hot stage. The progress of reactions was monitored, and the purity of the isolated compounds was checked, by TLC on Silufol UV-254 plates using acetone–hexane (3:5) as eluent; spots were visualized by treatment with iodine vapor and under UV light.

2-Acyl-4,5,6-trialkyl-3-aminothieno[2,3-*b*]pyridines 1a–1l (*general procedure*). A solution prepared from 0.23 g (10 mmol) of metallic sodium and 20 mL

of ethanol was added with stirring at 20°C to a mixture of 10 mmol of 1,3-diketone **2a**–**2c** and 1.0 g (10 mmol) of cyanothioacetamide (**3**) in 20 mL of DMF. The mixture was heated to 50°C, 10 mmol of α-halocarbonyl compound **4a**–**4l** was added, and the mixture was stirred at 20°C for 5 h and left to stand for 24 h. The mixture was diluted with an equal volume of water, and the precipitate was filtered off and washed in succession with water, ethanol, and hexane.

(3-Amino-4,6-dimethylthieno[2,3-*b*]pyridin-2-yl)(thiophen-2-yl)methanone (1a). Yield 2.2 g (77%), yellow rod-like crystals, mp 230–232°C (from AcOH). IR spectrum, ν, cm^{-1}: 3413, 3390, 3295 (NH_2), 1698 (C=O), 1648 (δ NH_2). ^1H NMR spectrum, δ, ppm: 2.47 s (3H, Me), 2.72 s (3H, Me), 7.07 s (1H, 5-H), 7.22–7.26 m (1H, 4′-H), 7.88–7.94 m (2H, 3′-H, 5′-H), 8.10 br.s (2H, NH_2). ^{13}C NMR spectrum, δ_C, ppm: 20.6, 24.4, 101.2, 121.7, 122.6, 128.9, 130.9, 133.2, 145.7, 146.4, 154.1, 161.5, 161.6, 179.3. Mass spectrum: *m*/*z* 289.0466 $[M + H]^+$. $C_{14}H_{12}N_2OS_2$. Calculated: *M* + H 289.0391.

(3-Amino-4,6-dimethylthieno[2,3-*b*]pyridin-2-yl)(4-chlorophenyl)methanone (1b). Yield 2.6 g (81%), yellow needles, mp 191–193°C (from AcOH). IR spectrum, ν, cm^{-1}: 3410–3305 (NH_2), 1684 (C=O). ^1H NMR spectrum, δ, ppm: 2.48 s (3H, Me), 2.73 s (3H, Me), 7.07 s (1H, 5-H), 7.57 d (2H, H_{arom}, *J* = 8.0 Hz), 7.74 d (2H, H_{arom}, *J* = 8.0 Hz), 8.06 br.s (2H, NH_2). ^{13}C NMR spectrum, δ_C, ppm: 20.6, 24.5, 102.5, 121.9, 122.5, 129.0 (2C), 129.7 (2C), 136.2, 140.0, 146.6, 153.5, 161.5, 162.1, 187.9. Mass spectrum: *m*/*z* 317.0514 $[M + H]^+$. $C_{16}H_{13}ClN_2OS$. Calculated: *M* + H 317.0437.

(3-Amino-4,6-dimethylthieno[2,3-*b*]pyridin-2-yl)(4-methoxyphenyl)methanone (1c). Yield 2.6 g (84%), yellow crystals fluorescing under UV light, mp 179–181°C (from AcOH). IR spectrum, ν, cm^{-1}: 3402–3298 (NH_2), 1700 (C=O). ^1H NMR spectrum, δ, ppm: 2.47 s (3H, Me), 2.73 s (3H, Me), 3.81 s (3H, MeO), 7.02 s (1H, 5-H), 7.05 d (2H, H_{arom}, *J* = 8.7 Hz), 7.73 d (2H, H_{arom}, *J* = 8.7 Hz), 7.93 br.s (2H, NH_2). ^{13}C NMR spectrum, δ_C, ppm: 20.5, 24.4, 55.8, 102.8, 114.1 (2C), 122.1, 122.4, 130.0 (2C), 133.8, 146.3, 158.8, 161.0, 161.8, 161.9, 188.5. Mass spectrum: *m*/*z* 313.1008 $[M + H]^+$. $C_{17}H_{16}N_2O_2S$. Calculated: *M* + H 313.0932.

Butyl 3-amino-4,6-dimethylthieno[2,3-*b*]pyridine-2-carboxylate (1d). Yield 2.0 g (72%), colorless cotton-like material fluorescinf under UV light, mp 118–120°C (from BuOH). IR spectrum, ν, cm^{-1}: 3418, 3388, 3005 (NH_2), 1722 (C=O), 1634 (δ NH_2). ^1H NMR spectrum, δ, ppm: 0.91 t (3H, Me, *J* = 7.4 Hz), 1.32–1.46 m (2H, CH_2), 1.57–1.74 m (2H, CH_2), 2.48 s (3H, Me), 2.71 s (3H, Me), 4.22 t (2H, OCH_2, *J* = 6.5 Hz), 6.76 br.s (2H, NH_2), 7.05 s (1H, 5-H). ^{13}C NMR spectrum, δ_C, ppm: 14.1, 19.2, 20.2, 24.3, 30.9, 64.1, 94.1, 122.2, 122.7, 145.5, 150.5, 160.0, 160.6, 165.3. Mass spectrum: *m*/*z* 279.0 (I_{rel} 100%) $[M + 1]^+$. Found, %: C 60.32; H 6.41; N 9.92. $C_{14}H_{18}N_2O_2S$. Calculated, %: C 60.41; H 6.52; N 10.06. *M* 278.4.

3-Amino-4,6-dimethyl-*N*-(1,3-thiazol-2-yl)-thieno[2,3-*b*]pyridine-2-carboxamide (1e). Yield 2.4 g (80%), light yellow plates fluorescing under UV light, mp 248–250°C (from BuOH); sublimes at 210°C to form to cubic crystals. IR spectrum, ν, cm^{-1}: 3418–3295 (NH, NH_2), 1673 (C=O), 1644 (δ NH_2). ^1H NMR spectrum, δ, ppm: 2.48 s (3H, Me), 2.72 s (3H, Me), 6.86–7.05 m (4H, 4′-H, 5′-H, NH_2), 7.41 s (1H, 5-H), 12.58 br.s (1H, CONH). ^{13}C NMR spectrum, δ_C, ppm: 20.3, 23.0, 93.9, 111.8, 115.1, 122.0 (2C), 128.8, 132.1, 145.1, 146.3, 159.3, 160.5. Mass spectrum: *m*/*z* 305.0526 $[M + H]^+$. $C_{13}H_{12}N_4OS_2$. Calculated: *M* + H 305.0453.

Propan-2-yl 3-amino-4,6-dimethylthieno[2,3-*b*]-pyridine-2-carboxylate (1f). Yield 2.0 g (77%), light yellow crystals fluorescing under UV light, mp 103–105°C (from *i*-PrOH). IR spectrum, ν, cm^{-1}: 3407–3300 (NH_2), 1719 (C=O), 1635 (δ NH_2). ^1H NMR spectrum, δ, ppm: 1.25 d (6H, Me, *J* = 6.2 Hz), 2.47 s (3H, Me), 2.68 s (3H, Me), 5.02–5.16 m (1H, OCH), 6.72 br.s (2H, NH_2), 7.01 s (1H, 5-H). ^{13}C NMR spectrum, δ_C, ppm: 20.2, 22.3 (2C), 24.3, 67.9, 94.5, 122.2, 122.7, 145.5, 150.3, 160.0, 160.5, 164.9. Mass spectrum: *m*/*z* 265.1006 $[M + H]^+$. $C_{13}H_{16}N_2O_2S$. Calculated: *M* + H 265.0932.

Propyl 3-amino-4,6-dimethylthieno[2,3-*b*]pyridine-2-carboxylate (1g). Yield 1.8 g (69%), yellow crystals fluorescing under UV light, mp 270–272°C (from PrOH). IR spectrum, ν, cm^{-1}: 3422–3295 (NH_2), 1715 (C=O), 1632 (δ NH_2). ^1H NMR spectrum, δ, ppm: 0.94 t (3H, Me, *J* = 7.4 Hz), 1.58–1.72 m (2H, CH_2), 2.49 s (3H, Me), 2.70 s (3H, Me), 4.17 t (2H, OCH_2, *J* = 6.6 Hz), 6.75 br.s (2H, NH_2), 7.03 s (1H, 5-H). ^{13}C NMR spectrum, δ_C, ppm: 10.8, 20.3, 22.3, 24.3, 65.8, 94.1, 122.3, 122.7, 145.6, 150.5, 160.1, 160.7, 165.4. Mass spectrum: *m*/*z* 265.2 (I_{rel} 100%) $[M + 1]^+$.

Found, %: C 58.96; H 5.96; N 10.48. $C_{13}H_{16}N_2O_2S$. Calculated, %: C 59.07; H 6.10; N 10.60. *M* 264.4.

***N*-(4-Acetylphenyl)-3-amino-4,6-dimethylthieno-[2,3-*b*]pyridine-2-carboxamide (1h).** Yield 2.8 g (83%), light yellow powder fluorescing under UV light, mp 222–224°C (from AcOH). IR spectrum, ν, cm^{-1}: 3412–3288 (NH_2), 1689 (C=O), 1674 (CONH), 1635 (δNH_2). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 2.49 s (3H, Me), 2.51 s (3H, Me), 2.69 s (3H, MeCO), 7.05 s (1H, 5-H), 7.07 br.s (2H, NH_2), 7.86 d (2H, H_{arom}, *J* = 8.8 Hz), 7.94 d (2H, H_{arom}, *J* = 8.8 Hz), 9.70 br.s (1H, CONH). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 20.4, 24.3, 26.9, 120.4 (2C), 122.5, 123.9, 129.5 (2C), 132.1, 144.1, 145.3, 150.9, 159.2, 159.8, 166.4, 184.6, 197.1. Mass spectrum: *m*/*z* 340.1115 $[M + H]^+$. $C_{18}H_{17}N_3O_2S$. Calculated: *M* + H 340.1041.

Octyl 3-amino-4,6-dimethylthieno[2,3-*b*]pyridine-2-carboxylate (1i). Yield 2.6 g (79%), colorless cotton-like material, mp 152–154°C (from EtOH). IR spectrum, ν, cm^{-1}: 3405–2284 (NH_2), 1698 (C=O), 1637 (δNH_2). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 0.83 t (3H, Me, *J* = 7.4 Hz), 1.19–1.46 m (10H, CH_2), 1.53–1.74 m (2H, CH_2), 2.48 s (3H, Me), 2.70 s (3H, Me), 4.19 t (2H, OCH_2, *J* = 6.3 Hz), 6.75 br.s (2H, NH_2), 7.02 s (1H, 5-H). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 14.4, 20.2, 22.5, 24.3, 25.9, 28.7, 28.9, 29.1, 31.6, 64.3, 119.2, 122.2, 123.0, 146.5, 151.4, 160.0, 160.6, 165.7. Mass spectrum: *m*/*z* 335.1785 $[M + H]^+$. $C_{18}H_{26}N_2O_2S$. Calculated: *M* + H 335.1715.

3-Amino-4,5,6-trimethyl-*N*-(2-methylphenyl)-thieno[2,3-*b*]pyridine-2-carboxamide (1j). Yield 2.3 g (70%), yellow crystals, mp 228–230°C (from BuOH), sublimes at 185°C. IR spectrum, ν, cm^{-1}: 3418–3305 (NH, NH_2), 1674 (CONH), 1633 (δNH_2). ^1H NMR spectrum, δ, ppm: 2.23 s (3H, Me), 2.24 s (3H, Me), 2.53 s (3H, Me), 2.66 s (3H, Me), 6.92 br.s (2H, NH_2), 7.15 t (1H, H_{arom}, *J* = 8.1 Hz), 7.20 t (1H, H_{arom}, *J* = 8.1 Hz), 7.26 d (1H, H_{arom}, *J* = 8.4 Hz), 7.29 d (1H, H_{arom}, *J* = 8.2 Hz), 9.13 br.s (1H, CONH). Mass spectrum: *m*/*z* 326.2 (I_{rel} 100%) $[M + 1]^+$. Found, %: C 66.29; H 5.74; N 12.85. $C_{18}H_{19}N_3OS$. Calculated, %: C 66.43; H 5.88; N 12.91. *M* 325.4.

3-Amino-5-ethyl-4,6-dimethyl-*N*-phenylthieno-[2,3-*b*]pyridine-2-carboxamide (1k). Yield 2.5 g (78%), yellow crystals, mp 236–238°C (from BuOH), sublimes at 170°C. IR spectrum, ν, cm^{-1}: 3440–3289 (NH, NH_2), 1688 (CONH), 1639 (δNH_2). ^1H NMR spectrum, δ, ppm: 1.10 t (3H, **Me**CH_2, *J* = 7.2 Hz), 2.58 s (3H, Me), 2.73 br.s (5H, Me, CH_2), 7.07 br.s (3H, H_{arom}, NH_2), 7.31 t (2H, H_{arom}, *J* = 7.6 Hz), 7.67 d (2H, H_{arom}, *J* = 7.9 Hz), 9.37 br.s (1H, CONH). ^{13}C NMR spectrum, δ_C, ppm: 14.0, 15.5, 21.6, 23.6, 97.5, 121.8 (2C), 123.9, 124.0, 128.8 (2C), 132.6, 139.3, 142.8, 150.1, 156,6, 158.2, 164.9. Mass spectrum: *m*/*z* 326.2 (I_{rel} 100%) $[M + 1]^+$. Found, %: C 66.32; H 5.78; N 12.84. $C_{18}H_{19}N_3OS$. Calculated, %: C 66.43; H 5.88; N 12.91. *M* 325.4.

(3-Amino-4,6-dimethylthieno[2,3-*b*]pyridin-2-yl)(4-bromophenyl)methanone (1l). Yield 2.9 g (75%), yellow crystals, mp 218–220°C (from dioxane). IR spectrum, ν, cm^{-1}: 3410–3300 (NH_2), 1698 (C=O), 1641 (δNH_2). ^1H NMR spectrum, δ, ppm: 1.19 t (3H, Me, *J* = 7.5 Hz), 2.68 s (3H, Me), 2.81 br.s (5H, Me, CH_2), 7.51 br.s (2H, NH_2), 7.61 d (2H, H_{arom}, *J* = 8.3 Hz), 7.73 d (2H, H_{arom}, *J* = 8.3 Hz). Mass spectrum: *m*/*z* 390.1 (I_{rel} 100%) $[M + 1]^+$. Found, %: C 55.39; H 4.36; N 7.05. $C_{18}H_{17}BrN_2OS$. Calculated, %: C 55.53; H 4.40; N 7.20. *M* 389.3.

7,8,9-Trimethylpyrido[3′,2′:4,5]thieno[3,2-*d*]pyrimidin-4-amine (6) was synthesized according to the procedure described above for compounds **1** using 1.2 mL (10 mmol) of 3-methylpentane-2,4-dione (**2b**) and 0.63 mL (10 mmol) of chloroacetonitrile (**5**). The precipitate was filtered off and mixed with 25 mL of formamide, and the mixture was refluxed for 2 h. After cooling to room temperature, the precipitate was filtered off and washed with ethanol and hexane. Yield 1.7 g (68%), colorless powder, mp 332–334°C (from AcOH). IR spectrum, ν, cm^{-1}: 3415–3307 (NH_2), 1642 (δNH_2). ^1H NMR spectrum, δ, ppm: 2.53 s (3H, Me), 2.56 s (3H, Me), 2.97 s (3H, Me), 7.44 br.s (2H, NH_2), 8.49 s (1H, 2-H). ^{13}C NMR spectrum, δ_C, ppm: 14.6, 15.1, 24.2, 112.0, 116.6, 124.1, 124.4, 145.0, 155.0, 155.6, 158.5, 158.8. Mass spectrum: *m*/*z* 245.0856 $[M + H]^+$. $C_{12}H_{12}N_4S$. Calculated: *M* + H 245.0783.

8′-Ethyl-7′,9′-dimethyl-1′*H*-spiro[cyclohexane-1,2′-pyrido[3′,2′:4,5]thieno[3,2-*d*]pyrimidine]-4′(3′*H*)-one (8) was synthesized according to the procedure described above for compounds **1** using 1.35 mL (10 mmol) of 3-ethylpentane-2,4-dione (**2c**) and 0.94 g (10 mmol) of chloroacetamide (**7**). The precipitate was filtered off and added to 25 mL of acetic acid, 1.0 mL (10 mmol) of cyclohexanone was added, and the mixture was refluxed for 3 h. After cooling to room temperature, the precipitate was filtered off and washed with ethanol and hexane. Yield 2.4 g (74%), colorless powder, mp 229–231°C (from AcOH). IR spectrum, ν, cm^{-1}: 3300 (NH), 1666 (CONH). ^1H NMR spectrum, δ, ppm: 1.09 t (3H, **Me**CH_2, *J* = 7.1 Hz), 1.22 br.s (2H, CH_2), 1.56 br.s (6H, CH_2), 2.03 br.s (2H, CH_2), 2.54 s (3H, Me), 2.57 s

(3H, Me), 2.73 q (2H, MeC**H**$_2$, J = 7.1 Hz), 5.87 br.s (1H, NH), 7.87 br.s (1H, CONH). Mass spectrum: m/z 330.2 (I_{rel} 100%) $[M + 1]^+$. Found, %: C 65.53; H 6.94; N 12.68. $C_{18}H_{23}N_3OS$. Calculated, %: C 65.62; H 7.04; N 12.75. M 329.5.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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