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New Version of Multicomponent Condensation Leading to 3-Amino-2-acyl-4,5,6-trimethylthieno[2,3-*b*]pyridines

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Abstract—3-Amino-2-acyl-4,5,6-trimethylthieno[2,3-*b*]pyridines were synthesized by multicomponent condensation of acetaldehyde, cyanothioacetamide, 4-(but-2-en-2-yl)-morpholine, and α-haloketones.

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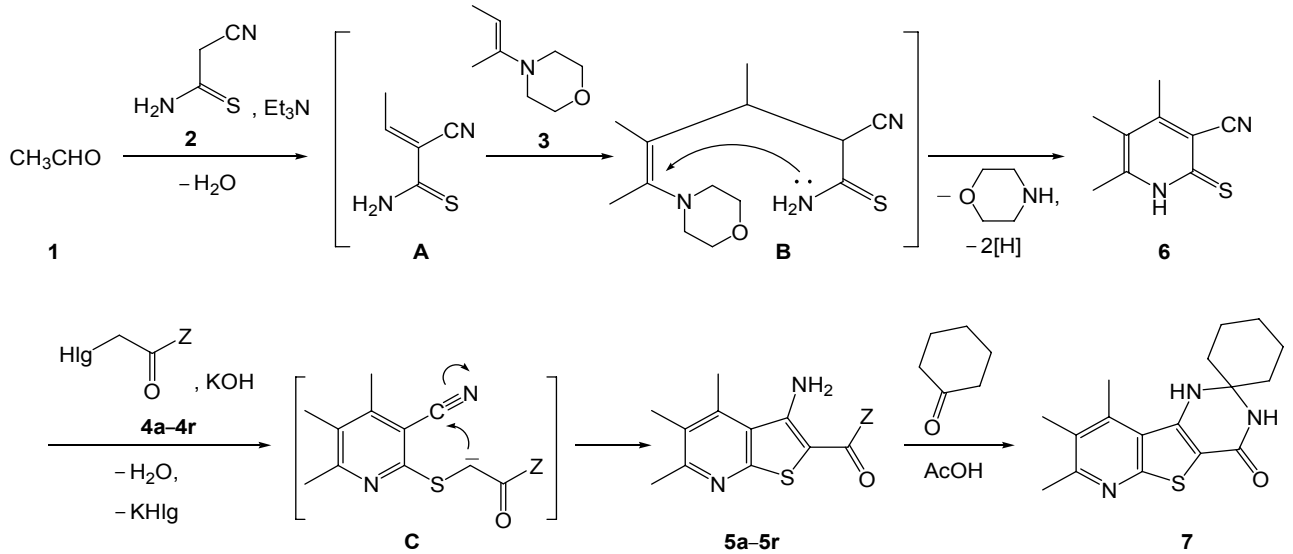
Derivatives of thieno[2,3-*b*]pyridines attract attention of researches for in this compounds series substances were found with antitumor [1–3], antibacterial[4, 5], and antistress [6, 7] activity. The principal method of their synthesis is intramolecular cyclization of 2-(alkylsulfanyl)pyridine-3-carbonitriles under effect of alkali [8–11].

We developed a method of synthesis of these compounds class based on multicomponent condensation of acetaldehyde **1**, cyanothioacetamide **2**, 4-(but-2-en-2-yl)morpholine **3**, and α-haloketones **4a–4r** in anhydrous ethanol at 20°C in the presence of triethylamine. The scheme of the synthesis of 3-amino-2-acyl-4,5,6-trimethylthieno[2,3-*b*]pyridines **5a–5r** includes evidently the generation as an intermediate of 2-cyanocrotonic acid thioamide **A**, a product of Knoevenagel reaction [12]. Further the alkylation occurs of enamine **3** with alkene **A** by Stork reaction [13] with the generation of intermediate **B** that in the reaction conditions undergoes an intramolecular nucleophilic vinyl substitution (S_NVin) [14–16] which can be logically regarded in this particular case as intramolecular reamination [17] and dehydration (probably under the effect of air oxygen) into 2-thioxo-4,5,6-trimethylpyridine-3-carbonitrile **6**. The last one was obtained previously by the condensation of 3-



4, Hlg = Cl (a, c–h, j–l, o, p), Br (b, i, m, n, q, r); **4**, **5**, Z =$PhCH_2O$ (**a**), 4-BrC_6H_4 (**b**), 4-BrC_6H_4NH (**c**), NH_2 (**d**), PhNH (**e**), 4-AcC_6H_4NH (**f**), $Me(CH_2)_7O$ (**g**), $Me(CH_2)_8O$ (**h**), 4-PhC_6H_4 (**i**), 4-MeC_6H_4NH (**j**), Me_2CHO (**k**), 4-$MeOC_6H_4NH$ (**l**), 2,4-$Me_2C_6H_3$ (**m**), 4-ClC_6H_4 (**n**), PrO (**o**), MeO (**p**), Me (**q**), 2,4-$(MeO)_2C_6H_3$ (**r**).

methylpenten-2,4-dione with cyanoacetamide in boiling ethanol in the presence of bases [18–21].

Further compound **6** in alkaline medium is alkylated regioselectively at the atom S with α-haloketones **4a–4r** giving thioethers **C** capable of easy transformation in the presence of bases into substituted 3-amino-2-acyl-4,5,6-trimethyltieno[2,3-*b*]-pyridines **5a–5r**.

At boiling 3-amino-4,5,6-trimethylthieno[2,3-*b*]pyridine-2-carboxamide **5d** with cyclohexanone in glacial acetic acid 7,8,9-trimethyl-2-spirocyclohexane-2,3-dihydropyrido[3',2':4,5]thieno[3,2-*d*]pyrimidin-4(1*H*)-one **7** was synthesized, a potential synthon for the preparation of antimicrobial drugs [22].

The composition and structure of compounds **5a–5r** and **7** is confirmed by physicochemical and spectral characteristics. In their IR spectra characteristic bands are present of stretching vibrations of carbonyl group at 1668–1718 cm^{-1} and stretching and bending vibrations of amino group at 3004–3319 and 1613–1649 cm^{-1} respectively. In the mass-spectra low intense peaks are observed of the fragment ions $[M + 2]^+$ confirming the presence of S atom in the molecules, and numeric value of molecular ion peak corresponds to «nitrogen rule» [23]. In ^{1}H NMR spectra the singlets of protons of three methyl groups are observed as singlets, and the signal of protons of amino group appears as broadened singlet in the region 6.63–8.13 ppm typical of such systems [24–26].

EXPERIMENTAL

IR spectra of synthesized compounds were recorded on a spectrophotometer Perkin Elmer Spectrum One in KBr pellets. ^{1}H NMR spectra were registered on a spectrometer Bruker-500 (500.13 MHz) in DMSO-d_6, internal reference TMS. Mass spectra of compounds **5a–5l** were obtained on an instrument MKh-1321 (EI, 70eV) with a direct admission of the sample into the ion source, of compounds **5m–5r**, **6**, and **7**, on a mass spectrometer Agilent1100 Series with a selective detector Agilent/MSDSL. The sample was admitted in a matrix CF_3COOH, ionization by electron impact (70 eV). Elemental analysis was performed on a CHN-analyzer Perkin Elmer. Melting points were measured on a Koeffler heating block. The reaction progress was monitored and the purity of compounds obtained was checked by TLC on Silufol UV-254 plates, eluent acetone–hexane, 3 : 5, development in iodine vapor or under UV irradiation.

3-Amino-2-acyl-4,5,6-trimethyltieno[2,3-*b*]pyridines (5a–5r). General method. A mixture of 0.6 mL (10 mmol) of freshly distilled acetaldehyde **1**, 1.0 g (10 mmol) of cyanothioacetamide **2**, and 1 drop of triethylamine in 20 mL of anhydrous ethanol at 20°C were stirred for 30 min, 1.4 g (10 mmol) of enamine **3** was added, the mixture was stirred for 2 h and left standing for 24 h. Then while stirring was added successively 5.6 mL (10 mmol) of 10% aqueous solution of KOH and 10 mmol of α-haloketone **4a–4r**, the mixture was stirred for 3 h, diluted with 15 mL of DMF, and again 5.6 mL (10 mmol) of 10% KOH solution was added. The reaction mixture was stirred for 30 min and diluted with equal amount of water. The precipitate was filtered off, washed with water, ethanol, and hexane.

Benzyl 3-amino-4,5,6-trimethylthieno[2,3-*b*]pyridine-2-carboxylate (5a). Yield 2.3 g (72%), colorless crystals, mp 119–121°C (AcOH), fluoresces under UV radiation. IR spectrum, cm^{-1}: 3318, 3280, 3197 [ν(NH_2)], 1711 [ν(C=O)], 1613 [δ(NH_2)]. ^{1}H NMR spectrum, δ, ppm: 2.28 s (3H, Me), 2.54 s (3H, Me), 2.68 s (3H, Me), 5.28 s (2H, CH_2), 6.67 br.s (2H, NH_2), 7.23 t (1H, Ph, *J* 6.9 Hz), 7.36 t (2H, Ph, *J* 6.9 Hz), 7.43 d (2H, Ph, *J* 7.0 Hz). Mass spectrum, *m/z* (I_{rel}, %): 328 (2) $[M + 2]^+$, 327 (7) $[M + 1]^+$, 326 (35) $[M]^+$, 312 (3) $[M - Me + 1]^+$, 282 (4), 218 (6), 217 (5), 192 (9), 191 (18), 92 (6) $[PhMe]^+$, 91 (100) $[PhCH_2]^+$, 77 (5) $[Ph]^+$, 65 (10). Found, %: C 66.08; H 5.41; N 8.44. $C_{18}H_{18}N_2O_2S$. Calculated, %: C 66.23; H 5.56; N 8.58. *M* 326.420.

(3-Amino-4,5,6-trimethylthieno[2,3-*b*]pyridin-2-yl)(4-bromophenyl)methanone (5b). Yield 3.0 g (79%), yellow cotton-like substance, mp 281–283°C (AcOH). IR spectrum, cm^{-1}: 3348, 3288, 3032 [ν(NH_2)], 1695 [ν(C=O)], 1637 [δ(NH_2)]. ^{1}H NMR spectrum, δ, ppm: 2.13 s (3H, Me), 2.56 s (3H, Me), 2.73 s (3H, Me), 7.62 d ($2H_{arom}$, *J* 7.5 Hz), 7.68 d ($2H_{arom}$, *J* 7.5 Hz), 8.13 br.s (2H, NH_2). Mass spectrum, *m/z* (I_{rel}, %): 377 (15) $[M + 2]^+$, 376 (63) $[M + 1]^+$, 375 (89) $[M]^+$, 374 (68) $[M - 1]^+$, 373 (100) $[M - 2]^+$, 360 (5) $[M - Me]^+$, 295 (8), 191 (9), 183 (12), 155 (17), 91 (4), 77 (9), 65 (5), 53 (6), 45 (7) $[CHS]^+$, 44 (4) $[S=S]^+$. Found, %: C 54.30; H 3.89; N 7.33. $C_{17}H_{15}BrN_2OS$. Calculated, %: C 54.41; H 4.03; N 7.46. *M* 375.290.

3-Amino-*N*-(4-bromophenyl)-4,5,6-trimethylthieno[2,3-*b*]pyridine-2-carboxamide (5c). Yield 3.0 g (80%), colorless powder, mp 208–210°C (BuOH), fluoresces under UV radiation. IR spectrum, cm^{-1}:

3339, 3211, 3190 [ν(NH, NH_2)], 1684 [ν(C=O)], 1639 [δ(NH_2)]. ^{1}H NMR spectrum, δ, ppm: 2.28 s (3H, Me), 2.54 s (3H, Me), 2.69 s (3H, Me), 6.90 br.s (2H, NH_2), 7.35 d (2H_{arom}, *J* 8.8 Hz), 7.68 d (2H_{arom}, *J* 8.8 Hz), 9.21 br.s (1H, NH). Mass spectrum, *m/z* (I_{rel}, %): 392 (3) $[M + 2]^+$, 391 (19) $[M + 1]^+$, 390 (4) $[M]^+$, 389 (20) $[M - 1]^+$, 219 (100) $[M - BrC_6H_4NH_2]^+$, 205 (6), 191 (14), 171 (3) $[M - BrC_6H_4NH_2]^+$, 155 (7), 91 (6) $[C_6H_4NH]^+$, 65 (4), 45 (3) $[CHS]^+$, 44 (6) $[S=S]^+$. Found, %: C 52.18; H 4.01; N 10.62. $C_{17}H_{16}BrN_3OS$. Calculated, %: C 52.32; H 4.13; N 10.77. *M* 390.305.

3-Amino-4,5,6-trimethylthieno[2,3-*b*]pyridine-2-carboxamide (5d). Yield 1.8 g (77%), colorless powder, mp 283–285°C (BuOH), sublimates at 200°C. IR spectrum, cm^{-1}: 3360, 3295, 3004 [ν(NH_2)], 1670 [ν(C=O)], 1631 [δ(NH_2)]. ^{1}H NMR spectrum, δ, ppm: 2.23 s (3H, Me), 2.52 s (3H, Me), 2.64 s (3H, Me), 6.86 br.s (2H, NH_2), 7.07 br.s (2H, $CONH_2$). Mass spectrum, *m/z* (I_{rel}, %): 237 (5) $[M + 2]^+$, 236 (13) $[M + 1]^+$, 235 (100) $[M]^+$, 218 (85) $[M - NH_3]^+$, 204 (9), 190 (63) $[M - NH_3 - CO]^+$, 175 (13), 163 (17), 146 (12), 131 (9), 118 (10), 104 (7), 91 (7), 77 (14), 65 (6), 53 (8), 45 (13) $[CHS]^+$, 44 (19) $[S=S]^+$, 39 (12). Found, %: C 52.00; H 5.40; N 17.71. $C_{11}H_{13}N_3OS$. Calculated, %: C 52.16; H 5.57; N 17.86. *M* 235.310.

3-Amino-*N*-phenyl-4,5,6-trimethylthieno[2,3-*b*]-pyridine-2-carboxamide (5e). Yield 2.5 g (81%), colorless powder, mp 275–277°C (BuOH). IR spectrum, cm^{-1}: 3337, 3270, 2980 [ν(NH, NH_2)], 1668 [ν(C=O)], 1642 [δ(NH_2)]. ^{1}H NMR spectrum, δ, ppm: 2.27 s (3H, Me), 2.55 s (3H, Me), 2.70 s (3H, Me), 6.88 br.s (2H, NH_2), 7.04 t (1H, Ph, *J* 7.6 Hz), 7.28 t (2H, Ph, *J* 7.6 Hz), 7.67 d (2H, Ph, *J* 7.7 Hz), 9.26 br.s (1H, NH). Mass spectrum, *m/z* (I_{rel}, %): 313 (3) $[M + 2]^+$, 312 (7) $[M + 1]^+$, 311 (38) $[M]^+$, 219 (100) $[M - PhNH_2]^+$, 205 (7), 191 (16), 147 (8), 93 (11) $[PhNH_3]^+$, 77 (8) $[Ph]^+$, 65 (6), 45 (4) $[CHS]^+$, 44 (8) $[S=S]^+$. Found, %: C 65.42; H 5.41; N 13.33. $C_{17}H_{17}N_3OS$. Calculated, %: C 65.57; H 5.50; N 13.49 *M* 311.408.

3-Amino-*N*-(4-acetylphenyl)-4,5,6-trimethylthieno[2,3-*b*]pyridine-2-carboxamide (5f). Yield 2.6 g (75%), yellow powder, mp 265–267°C (BuOH). IR spectrum, cm^{-1}: 3319, 3280, 3004 [ν(NH, NH_2)], 1670 [ν(C=O)], 1633 [δ(NH_2)]. ^{1}H NMR spectrum, δ, ppm: 2.31 s (3H, Me), 2.43 s (3H, Me), 2.54 s (3H, Me), 2.71 s (3H, MeCO), 6.96 br.s (2H, NH_2), 7.85 d (2H_{arom}, *J* 7.2 Hz), 7.94 d (2H_{arom}, *J* 7.2 Hz), 9.34 br.s (1H, NH). Mass spectrum, *m/z* (I_{rel}, %): 355 (2) $[M + 2]^+$, 354 (8) $[M + 1]^+$, 353 (32) $[M]^+$, 219 (100) $[M - AcC_6H_4NH]^+$, 191 (16) $[M - AcC_6H_4NHCO]^+$, 169 (12), 147 (8), 120 (7), 73 (9), 65 (5), 44 (11) $[C=S]^+$. Found, %: C 64.42; H 5.30; N 11.77. $C_{19}H_{19}N_3O_2S$. Calculated, %: C64.57; H5.42; N11.89. *M* 353.446.

Octyl 3-amino-4,5,6-trimethylthieno[2,3-*b*]pyridine-2-carboxylate (5g). Yield 2.4 g (68%), colorless powder, mp 121–123°C (EtOH). IR spectrum, cm^{-1}: 3333, 3280, 3008 [ν(NH_2)], 1714 [ν(C=O)], 1641 [δ(NH_2)]. ^{1}H NMR spectrum, δ, ppm: 0.88 t (3H, Me, *J* 6.2 Hz), 1.26-1.49 m (10H, 5CH_2), 1.67–1.78 m (2H, CH_2), 2.28 s (3H, Me), 2.54 s (3H, Me), 2.69 s (3H, Me), 4.20 t (2H, OCH_2, *J* 5.8 Hz), 6.63 br.s (2H, NH_2). Mass spectrum, *m/z* (I_{rel}, %): 350 (5) $[M + 2]^+$, 349 (18) $[M + 1]^+$, 348 (89) $[M]^+$, 334 (10), 236 (48) $[M - NH_3 - Me(CH_2)_7O]^+$, 218 (100) $[M - Me(CH_2)_7OH]^+$, 204 (18), 190 (26), 149 (13), 77 (6), 55 (12), 41 (28). Found, %: C 65.33; H 7.96; N 7.91. $C_{19}H_{28}N_2O_2S$. Calculated, %: C 65.48; H 8.10; N 8.04. *M* 348.511.

Nonyl 3-amino-4,5,6-trimethylthieno[2,3-*b*]pyridine-2-carboxylate (5h). Yield 2.5 g (70%), colorless powder, mp 113–115°C (MeOH). IR spectrum, cm^{-1}: 3342, 3277, 3118 [ν(NH_2)], 1706 [ν(C=O)], 1639 [δ(NH_2)]. ^{1}H NMR spectrum, δ, ppm: 0.87 t (3H, Me, *J* 6.4 Hz), 1.23-1.46 m (12H, 6CH_2), 1.66-1.78 m (2H, CH_2), 2.29 s (3H, Me), 2.55 s (3H, Me), 2.68 s (3H, Me), 4.21 t (2H, OCH_2, *J* 5.1Hz), 6.53 br.s (2H, NH_2). Mass spectrum, *m/z* (I_{rel}, %): 364 (5) $[M + 2]^+$, 363 (23) $[M + 1]^+$, 362 (100) $[M]^+$, 348 (12), 236 (49) $[M - Me(CH_2)_7CH]^+$, 219 (36) $[M - Me(CH_2)_8O]^+$, 218 (91) $[M - Me(CH_2)_8OH]^+$, 204 (13), 190 (21), 55 (11), 43 (20), 41 (21). Found, %: C 66.18; H 8.22; N 7.60. $C_{20}H_{30}N_2O_2S$. Calculated, %: C 66.26; H 8.34; N 7.73. *M* 362.538.

(3-Amino-4,5,6-trimethylthieno[2,3-*b*]pyridin-2-yl)(biphenyl-4-yl)methanone (5i). Yield 3.2 g (85%), yellow powder, mp 259–261°C (AcOH). IR spectrum, cm^{-1}: 3321, 3295, 3204 [ν(NH_2)], 1699 [ν(C=O)], 1636 [δ(NH_2)]. ^{1}H NMR spectrum, δ, ppm: 2.32 s (3H, Me), 2.56 s (3H, Me), 2.78 s (3H, Me), 7.47 br.s (2H, NH_2), 7.61-7.78 m (5H_{arom}), 7.86 d (2H_{arom}, *J* 7.7 Hz), 8.06 d (2H_{arom}, *J* 7.1 Hz). Mass spectrum, *m/z* (I_{rel}, %): 374 (4) $[M + 2]^+$, 373 (16) $[M + 1]^+$, 372 (57) $[M]^+$, 371 (100) $[M - 1]^+$, 355 (61) $[M - NH_3]^+$, 295 (4), 181 (9), 172 (8), 152 (39) $[PhC_6H_3]^+$, 73 (8), 44 (15) $[C=S]^+$. Found, %: C 74.06; H 5.32; N 7.40. $C_{23}H_{20}N_2OS$. Calculated, %: C 74.16; H 5.41; N 7.52. *M* 372.491.

3-Amino-*N*-(2-methylphenyl)-4,5,6-trimethylthieno[2,3-*b*]pyridine-2-carboxamide (5j). Yield 2.6 g (79%), light-green powder, mp 248–250°C (BuOH). IR spectrum, cm^{-1}: 3330, 3280, 3195 [ν(NH, NH_2)], 1668 [ν(C=O)], 1635 [δ(NH_2)]. ^1H NMR spectrum, δ, ppm: 2.22 s (3H, Me), 2.31 s (3H, Me), 2.58 s (3H, Me), 2.71 s (3H, Me), 6.76 br.s (2H, NH_2), 7.09 t ($1H_{arom}$, *J* 7.2 Hz), 7.17 t ($1H_{arom}$, *J* 6.9 Hz), 7.20 d ($1H_{arom}$, *J* 7.4 Hz), 7.49 d ($2H_{arom}$, *J* 7.5 Hz), 8.56 br.s (1H, NH). Mass spectrum, *m/z* (I_{rel}, %): 327 (4) $[M + 2]^+$, 326 (13) $[M + 1]^+$, 325 (55) $[M]^+$, 219 (100) $[M - MeC_6H_4NH]^+$, 205 (5), 107 (14) $[MeC_6H_4NH_2]^+$, 91 (4) $[MeC_6H_4]^+$, 45 (3) $[CHS]^+$. Found, %: C 66.35; H 5.77; N 12.82. $C_{18}H_{19}N_3OS$. Calculated, %: C 66.43; H 5.89; N 12.91. *M* 325.435.

Isopropyl 3-amino-4,5,6-trimethylthieno[2,3-*b*]pyridine-2-carboxylate (5k). Yield 2.0 g (70%), colorless lamellar crystals, mp 181–183°C (*i*-PrOH). IR spectrum, cm^{-1}: 3348, 3295, 3007 [ν(NH_2)], 1711 [ν(C=O)], 1647 [δ(NH_2)]. ^1H NMR spectrum, δ, ppm: 1.34 d (6H, Me, *J* 5.0 Hz), 2.26 s (3H, Me), 2.52 s (3H, Me), 2.66 s (3H, Me), 5.02–5.23 m (1H, CHO), 7.61 br.s (2H, NH_2). Mass spectrum, *m/z* (I_{rel}, %): 280 (3) $[M + 2]^+$, 279 (6) $[M + 1]^+$, 278 (38) $[M]^+$, 264 (4), 236 (42) $[M - CMe_2]^+$, 218 (100) $[M - CHMe_2 - NH_3]^+$, 204 (11), 190 (32), 175 (7), 146 (8), 77 (8), 44 (14) $[C=S]^+$, 41 (16). Found, %: C 60.28; H 6.41; N 9.88. $C_{14}H_{18}N_2O_2S$. Calculated, %: C 60.41; H 6.52; N 10.06. *M* 278.375.

3-Amino-*N*-(4-methoxyphenyl)-4,5,6-trimethylthieno[2,3-*b*]pyridine-2-carboxamide (5l). Yield 2.6 g (76%), colorless powder, mp 271–273°C (BuOH). IR spectrum, cm^{-1}: 3330, 3300, 3244 [ν(NH, NH_2)], 1670 [ν(C=O)], 1638 [δ(NH_2)]. ^1H NMR spectrum, δ, ppm: 2.29 s (3H, Me), 2.56 s (3H, Me), 2.70 s (3H, Me), 3.75 s (3H, MeO), 6.79 br.s (2H, NH_2), 6.85 d ($2H_{arom}$, *J* 7.9Hz), 7.57 d ($2H_{arom}$, *J* 7.9 Hz), 9.10 br.s (1H, NH). Mass spectrum, *m/z* (I_{rel}, %): 343 (2) $[M + 2]^+$, 342 (6) $[M + 1]^+$, 341 (39) $[M]^+$, 219 (52) $[M - MeOC_6H_4NH]^+$, 191 (10), 123 (100) $[MeOC_6H_4NH_2]^+$, 108 (17), 44 (7) $[C=S]^+$, 41 (4). Found, %: C 63.25; H 5.49; N 12.18. $C_{18}H_{19}N_3O_2S$. Calculated, %: C 63.32; H 5.61; N 12.31. *M* 341.435.

(3-Amino-4,5,6-trimethylthieno[2,3-*b*]pyridin-2-yl)(2,4-dimethylphenyl)methanone (5m). Yield 2.4 g (73%), yellow powder, mp 205–207°C (AcOH). IR spectrum, cm^{-1}: 3318, 3295, 3204 [ν(NH_2)], 1702 [ν(C=O)], 1642 [δ(NH_2)]. ^1H NMR spectrum, δ, ppm: 2.18 s (3H, Me), 2.22 s (3H, Me), 2.34 s (3H, Me), 2.41 s (3H, Me), 2.68 s (3H, Me), 6.84 br.s (2H, NH_2), 6.99 s ($1H_{arom}$), 7.14 d ($1H_{arom}$, *J* 7.7 Hz), 7.82 d ($1H_{arom}$, *J* 7.7 Hz). Mass spectrum, *m/z* (I_{rel}, %): 325 (100) $[M + 1]^+$. Found, %: C 70.21; H 6.09; N 8.50. $C_{19}H_{20}N_2OS$. Calculated, %: C 70.34; H 6.21; N 8.63. *M* 324.447.

(3-Amino-4,5,6-trimethylthieno[2,3-*b*]pyridin-2-yl)(4-chlorophenyl)mehanone (5n). Yield 2.5 g (75%), yellow powder, mp 137–139°C (AcOH). IR spectrum, cm^{-1}: 3330, 3295, 3200 [ν(NH_2)], 1688 [ν(C=O)], 1648 [δ(NH_2)]. ^1H NMR spectrum, δ, ppm: 2.23 s (3H, Me), 2.51 s (3H, Me), 2.67 s (3H, Me), 7.55 d ($2H_{arom}$, *J* 8.6 Hz), 7.73 d ($2H_{arom}$, *J* 8.6 Hz). Mass spectrum, *m/z* (I_{rel}, %): 331 (100) $[M + 1]^+$. Found, %: C 61.62; H 4.39; N 8.35. $C_{17}H_{15}ClN_2OS$. Calculated, %: C 61.72; H 4.57; N 8.47. *M* 330.839.

Propyl 3-amino-4,5,6-trimethylthieno[2,3-*b*]pyridine-2-carboxylate (5o). Yield 2.0 g (70%), yellow crystals, mp 150–152°C (PrOH). IR spectrum, cm^{-1}: 3322, 3281, 3190 [ν(NH_2)], 1714 [ν(C=O)], 1648 [δ(NH_2)]. ^1H NMR spectrum, δ, ppm: 0.96 t (3H, Me, *J* 6.5 Hz), 1.55-1.87 m (2H, CH_2), 2.24 s (3H, Me), 2.53 s (3H, Me), 2.66 s (3H, Me), 4.19 t (2H, OCH_2, *J* 6.2 Hz), 6.84 br.s (2H, NH_2). Mass spectrum, *m/z* (I_{rel}, %): 279 (100) $[M + 1]^+$. Found, %: C 60.25; H 6.44; N 9.96. $C_{14}H_{18}N_2O_2S$. Calculated, %: C 60.41; H 6.52; N 10.06. *M* 278.375.

Methyl 3-amino-4,5,6-trimethylthieno[2,3-*b*]pyridine-2-carboxylate (5p). Yield 1.9 g (69%), colorless cotton-like crystals, mp 160–162°C (MeOH). IR spectrum, cm^{-1}: 3310, 3285, 3170 [ν(NH_2)], 1718 [ν(C=O)], 1641 [δ(NH_2)]. ^1H NMR spectrum, δ, ppm: 2.26 s (3H, Me), 2.52 s (3H, Me), 2.66 s (3H, Me), 3.80 s (3H, Me), 6.71 br.s (2H, NH_2). Mass spectrum, *m/z* (I_{rel}, %): 251 (100) $[M + 1]^+$. Found, %: C 57.47; H 5.52; N 11.02. $C_{12}H_{14}N_2O_2S$. Calculated, %: C 57.58; H 5.64; N 11.19. *M* 250.322.

1-(3-Amino-2-acetyl-4,5,6-trimethylthieno[2,3-*b*]pyridin-2-yl)ethanone (5q). Yield 1.7 g (72%), yellow powder, fluoresces under UV radiation, mp 200–202°C (AcOH). IR spectrum, cm^{-1}: 3351, 3315, 2264 [ν(NH_2)], 1713 [ν(C=O)], 1649 [δ(NH_2)]. ^1H NMR spectrum, δ, ppm: 2.23 s (3H, Me), 2.32 s (3H, Me), 2.52 s (3H, Me), 2.64 s (3H, Me), 7.71 br.s (2H, NH_2). Mass spectrum, *m/z* (I_{rel}, %): 235 (100) $[M + 1]^+$. Found, %: C 61.42; H 5.94; N 11.80. $C_{12}H_{14}N_2OS$. Calculated, %: C 61.51; H 6.02; N 11.96. *M* 234.322.

(3-Amino-4,5,6-trimethylthieno[2,3-*b*]pyridin-2-yl)(2,4-dimethoxyphenyl)methanone (5r). Yield 2.8 g

(80%), yellow powder, mp 215–217°C (AcOH). IR spectrum, cm^{-1}: 3352, 3300, 3248 [ν(NH_2)], 1694 [ν(C=O)], 1649 [δ(NH_2)]. ^1H NMR spectrum, δ, ppm: 2.29 s (3H, Me), 2.52 s (3H, Me), 2.70 s (3H, Me), 3.85 s (3H, MeO), 3.98 s (3H, MeO), 6.69 s ($1H_{arom}$), 7.41 d ($1H_{arom}$, *J* 7.9 Hz), 7.64 d ($1H_{arom}$, *J* 7.9 Hz), 7.80 br.s (2H, NH_2). Mass spectrum, *m/z* (I_{rel}, %): 357 (100) $[M + 1]^+$. Found, %: C 63.91; H 5.55; N 7.72. $C_{19}H_{20}N_2O_3S$. Calculated, %: C 64.02; H 5.66; N 7.86. *M* 356.446.

4,5,6-Trimethyl-2-thioxo-1,2-dihydropyridine-3-carbonitrile (6). To reaction mixture of 0.6 mL (10 mmol) of freshly distilled acetaldehyde **1** and 1.0 g (10 mmol) of cyanothioacetamide **2** in 20 mL of anhydrous ethanol at 20°C was added 1 drop of triethylamine and the mixture was stirred for 30min till full dissolution of CH-acid **2**, then 1.4 g (10 mmol) of enamine **3** was added, the mixture was stirred for 1 h and left standing for 24 h. The reaction mixture was diluted with 10% HCl solution to pH 3 and left standing for 5 h. The precipitate was filtered off, washed with ethanol and hexane. Yield 1.4 g (79%), yellow crystalline powder, mp 268–270°C (AcOH), sublimates at 220°C (mp 276–279°C [10]). ^1H NMR spectrum, δ, ppm: 2.01 s (3H, Me), 2.30 s (3H, Me), 2.38 s (3H, Me), 13.62 br.s (1H, NH). Mass spectrum, *m/z* (I_{rel}, %): 179 (100) $[M + 1]^+$. $C_9H_{10}N_2S$. *M* 178.257.

2-Spirocyclohexane-7,8,9-trimethyl-2,3-dihydropyrido[3',2':4,5]thieno[3,2-*d*]pyrimidin-4(1*H*)-one (7). A mixture of 2.3 g (10 mmol) of substituted thienopyridine **5d** and 1.0 mL (10 mmol) of cyclohexanone in 20 mL of glacial acetic acid was boiled for 4 h and left standing for 24 h. The precipitate was filtered off and washed with ether. Yield 2.5 g (78%), yellow powder, mp 240–242°C (AcOH), fluoresces under UV radiation. IR spectrum, ν, cm^{-1}: 3330 (NH), 1665 (CONH). ^1H NMR spectrum, δ, ppm: 1.21–1.26 m (1H of cyclohexane), 1.28–1.33 m (7H of cyclohexane), 2.02-2.14 m (2H of cyclohexane), 2.27 s (3H, Me), 2.54 s (3H, Me), 2.69 s (3H, Me), 5.60 br.s (1H, NH), 7.69 br.s (1H, NHCO). Mass spectrum, *m/z* (I_{rel}, %): 316 (100) $[M + 1]^+$. Found, %: C 64.65; H 6.61; N 13.18. $C_{17}H_{21}N_3OS$. Calculated, %: C 64.73; H 6.71; N 13.32. *M* 315.440.

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