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New Multicomponent Synthesis of Functionalized Nitriles and Esters of 6-Alkylsulfanyl-1,4-dihydronicotinic Acids

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Abstract—The multicomponent condensation of malononitrile, hydrogen sulfide, aryl or hetaryl aldehydes, 1,3-dicarbonyl compounds and alkylating reagents afforded functionalized nitriles and esters of 6-alkylsulfanyl-1,4-dihydronicotinic acids, their aromatic analogues and 1,4-dihydrothieno[2,3-*b*]pyridines.

Keywords: malononitrile, (het)aryl aldehydes, 1,3-dicarbonyl compounds, 1,4-dihydrothieno[2,3-*b*]pyridines, [3,3]-sigmatropic rearrangement

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Nicotinic acid derivatives are promising in the development of drugs for the treatment of cardiovascular [1–3], pulmonary [4], antitumor [5] diseases and HIV [6]. They can be used in electron-graphic toners as electric charge regulators [7] and in positive photosensitive compositions [8].

In continuation of research in the field of nicotinic acid chemistry [9–11], we investigated a new version of multicomponent condensation, leading to the formation of functionalized nitriles and esters of 1,4-dihydronicotinic acid. It was found that the reaction of malononitrile **1**, hydrogen sulfide **2**, aryl or hetaryl aldehydes **3a**–**3c** and 1,3-dicarbonyl compounds **4a**–**4c** produces nicotinic acid derivatives, namely ammonium 1,4-dihydropyridine-2-thiolates **5a**, **5b** and ethyl 5-cyano-2-methyl-4-(3-methylthiophen-2-yl)-6-thioxo-1,4,5,6-tetrahydropyridinecarboxylate **6** (Scheme 1). Recrystallization of salt **5a** from glacial acetic acid gave ethyl 2-propyl-6-thioxo-4-(furan-2-yl)-5-cyano-1,6-dihydropyridine-3-carboxylate **7**. Condensation took place in ethanol at 20°C under catalysis with aliphatic amines (triethylamine or morpholine).

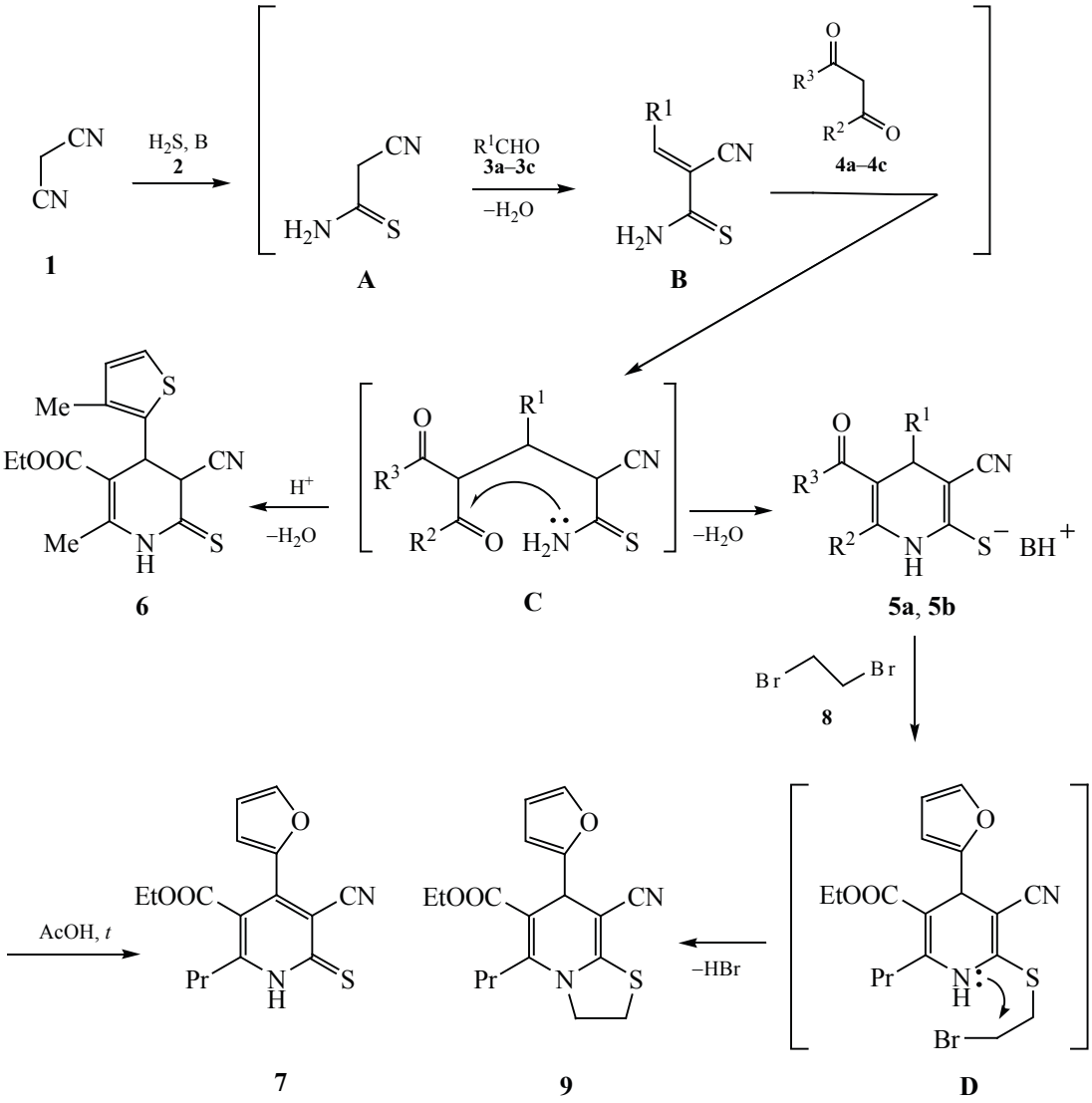
An increase in the number of components of this condensation, in particular, the addition of 1,2-dibromoethane **8** as an alkylating reagent, led to the formation of ethyl 5-propyl-7-(furan-2-yl)-8-cyano-3,7-dihydro-2*H*-thiazolo[3,2-*a*]pyridine-6-carboxylate **9** (Scheme 1).

The reaction scheme includes the formation of cyanothioacetamide **A**, which undergoes Knoevenagel-type condensation with aldehydes **3a–3c** to form the corresponding alkenes **B**. Subsequently, the Michael addition of CH acids **4a–4c** to aryl(hetaryl)methylidene cyanothioacetamides **B** to form adducts **C**. The latter are unstable under the reaction conditions and chemoselectively transform into salts **5a**, **5b**. In an acidic medium, they easily form partially hydrogenated pyridine-6-thiones **6** and **7**. The introduction of an equimolar amount of 1,2-dibromethane **8** into this reaction in the presence of a 10% aqueous KOH solution led to double alkylation of salt **5a**. The initially formed thioether **D** under the reaction conditions was intramolecularly alkylated at the nitrogen atom of the dihydropyridine core, resulting in the formation of a partially hydrogenated thiazolo[3,2-*a*]pyridine **9** (Scheme 1).

The involvement into this multicomponent condensation of 1,2-dibromoethane **8** as an alkylating reagent in a 0.5 mol amount led to the formation of 1,2-bis(1,4-dihydropyridin-6-ylsulfanyl)ethanes **10a**, **10b** and diethyl 6,6'-[ethane-1,2-diylbis(sulfanediyl)]bis[5-cyano-4-(furan-2-yl)-2-propylnicotinate] **11**, respectively (Scheme 2).

The use of monohaloalkylating reagents **12a**–**12h** in this reaction under the same conditions allows the synthesis of 6-alkylsulfanyl-1,4-dihydronicotinic acid esters **13a**–**13g** and nicotinic acid esters **14a**, **14b**. Increasing the basicity of the reaction mixture by adding

Scheme 1.



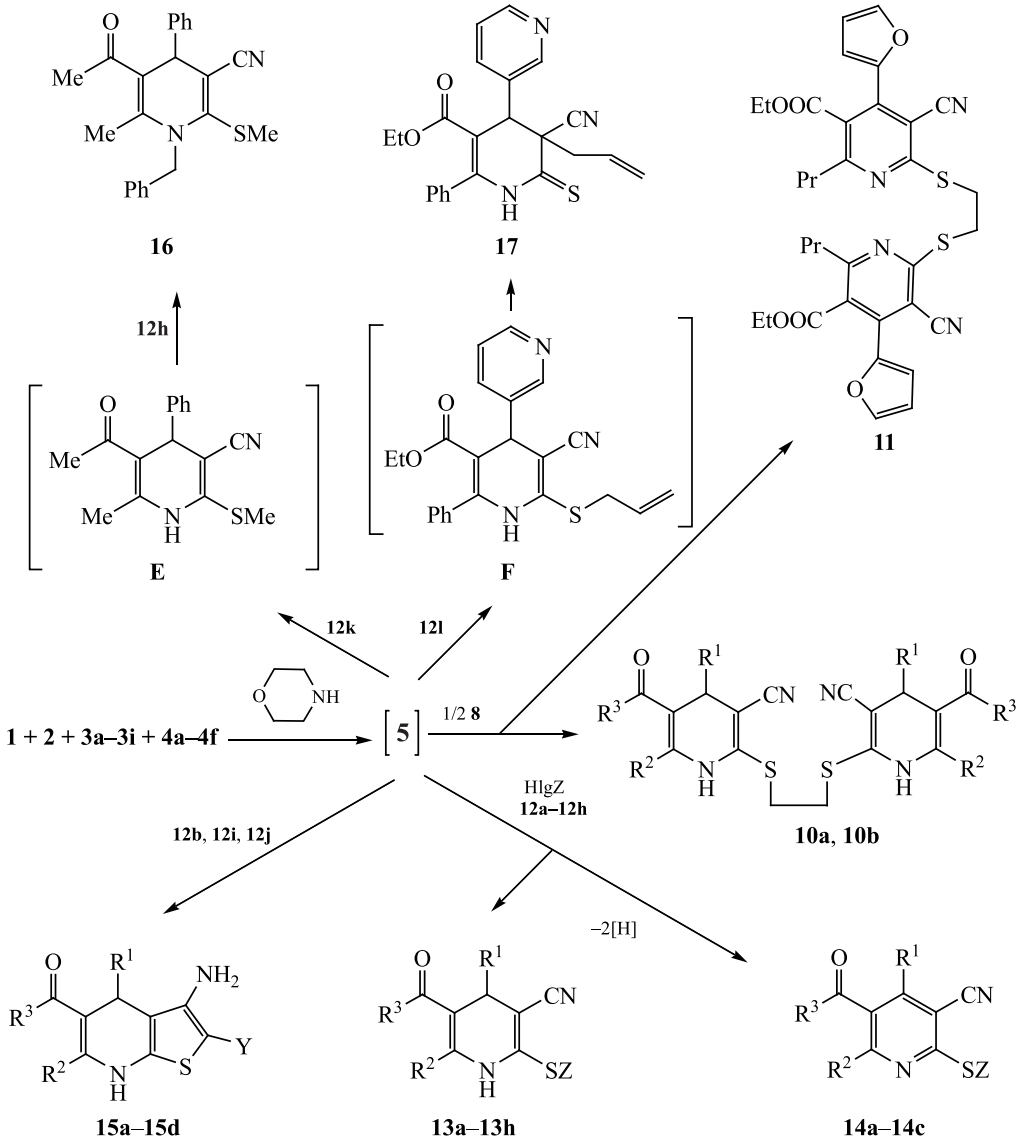
B = Et_3N, morpholine; R^1 = furan-2-yl (**3a**), 5-methylfuran-2-yl (**3b**), 3-methylthiophen-2-yl (**3c**); R^2 = Pr, R^3 = OEt (**4a**); Me, OEt (**4b**); Me, Me (**4c**); R^1 = furan-2-yl, R^2 = Pr, R^3 = OEt, B = Et_3N (**5a**); R^1 = 5-methylfuran-2-yl, R^2 = R^3 = Me, B = morpholine (**5b**).

a 10% aqueous KOH solution after the stage of adding alkyl halides **12b**, **12i**, and **12j** led to other reaction outcome. The intermediately formed thioesters **13** underwent intramolecular cyclization into substituted 1,4-dihydrothieno[2,3-*b*]pyridines **15a**–**15d**. The latter are promising intermediates for the development of antitumor [12–15] and antimicrobial agents [16, 17], as well as for the treatment of diseases of the central nervous system [18].

The consecutive use of two different alkylating reagents, methyl iodide **12k** and benzyl chloride **12h**, in the condensation of malononitrile **1**, hydrogen sulfide **2**, benzaldehyde **3i**, ethyl benzoylacetate **4d** and morpholine led to the formation of 5-acetyl-1-benzyl-6-methyl-4-phenyl-1,4-dihydronicotinonitrile **16**. It is logical to assume the formation in the reaction mixture of a fully substituted 1,4-dihydropyridine **E** as an intermediate.

Unlike the above examples, the multicomponent condensation of malononitrile **1**, hydrogen sulfide **2**, 3-pyridinecarbaldehyde **3f**, ethyl benzoylacetate **4d**, morpholine and allyl bromide **12l** proceeded unusually. It is not possible to isolate the expected corresponding

Scheme 2.



R^1 = 2-$MeOC_6H_4$ (**3d**), 2-Me-4-FC_6H_3 (**3e**), pyridine-3-yl (**3f**), 2-ClC_6H_4 (**3g**), 4-ClC_6H_4 (**3h**), Ph (**3i**); R^2= Ph, R^3 = OEt (**4d**); R^2 = *i*-Pr, R^3 = MeO (**4e**); R^2 = Me, R^3 = CH_2=$CHCH_2O$ (**4f**); R^1 = 3-methylthiene-2-yl, R^2 = Me, R^3 = OEt (**10a**); R^1 = 2-$MeOC_6H_4$, R^2 = Ph, R^3 = OEt (**10b**); Hlg = Br, Z = 4-$ClC_6H_4C(O)CH_2$ (**12a**); Hlg = Cl, Z = $CH_2C(O)NH_2$ (**12b**); Hlg = Br, Z = cumarine-3-ylcarbonylmethylene (**12c**); Hlg = Cl, Z = 2-$MeC_6H_4NHC(O)CH_2$ (**12d**); Hlg = Br, Z = CH(COPh)(*i*-Pr) (**12e**); Hlg = Br, Z = cyclohex-2-en-1-yl (**12f**); Hlg = Br, Z = $CH_2C{\equiv}CH$ (**12g**); Hlg = Cl, Z = CH_2Ph (**12h**); Hlg = Cl, Z = $PhCH_2C(O)OCH_2$ (**12i**); Hlg = Cl, Z = thiazole-2-ylcarbamoylmethylene (**12j**); Hlg = I, Z = Me (**12k**); Hlg = Br, Z = CH_2=$CHCH_2$ (**12l**); R^1 = 2-Me-4-FC_6H_3, R^2 = *i*-Pr, R^3 = MeO, Z = 4-$ClC_6H_4C(O)CH_2$ (**13a**); R^1 = 2-Me-4-FC_6H_3, R^2 = *i*-Pr, R^3 = MeO, Z = $CH_2C(O)NH_2$ (**13b**); R^1 = 2-Me-4-FC_6H_3, R^2 = *i*-Pr, R^3 = MeO, Z = cumarine-3-ylcarbonylmethylene (**13c**); R^1 = fur-2-yl, R^2 = Me, R^3 = CH_2=$CHCH_2O$, Z = 2-$MeC_6H_4NHC(O)CH_2$ (**13d**); R^1 = 2-$MeOC_6H_4$, R^2 = Ph, R^3 = OEt, Z = CH(COPh)(*i*-Pr) (**13e**); R^1 = pyridine-3-yl, R^2 = Ph, R^3 = OEt, Z = cyclohex-2-en-1-yl (**13f**); R^1 = 2-ClC_6H_4, R^2 = R^3 = Me, Z = cyclohex-2-en-1-yl (**13g**); R^1 = pyridine-3-yl, R^2 = Ph, R^3 = OEt, Z = $CH_2C{\equiv}CH$ (**13h**); R^1 = 5-methylfur-2-yl, R^2 = Me, R^3 = Me, Z = $CH_2C{\equiv}CH$ (**14a**), R^1 = 4-ClC_6H_4, R^2 = R^3 = Me, CH_2Ph (**14b**); R^1 = fur-2-yl, R^2 = Pr, R^3 = OEt, Z = cumarine-3-ylcarbonylmethylene (**14c**); R^1 = pyridine-3-yl, R^2 = Ph, R^3 = OEt, Y = $C(O)NH_2$ (**15a**); R^1 = 3-methylthiene-2-yl, R^2 = Me, R^3 = OEt, Y = $C(O)NH_2$ (**15b**); R^1 = pyridine-3-yl, R^2 = Ph, R^3 = OEt, Y = $PhCH_2C(O)O$ (**15c**); R^1 = fur-2-yl, R^2 = Me, R^3 = CH_2=$CHCH_2O$, Y = thiazole-2-ylcarbamoylmethylene (**15d**).

thioether **F** due to easy [3,3] sigmatropic rearrangement into ethyl 5'-allyl-5'-cyano-2'-phenyl-6'-thioxo-1',4',5',6'-tetrahydro-[3',4'-bipyridine]-3-carboxylate **17** (Scheme 2).

Confirmation of the implementation of the above rearrangement is the presence in the IR spectrum of the obtained compounds of the characteristic absorption band of stretching vibrations of the non-conjugated cyano group at 2244 cm^{-1}. In the ^1H NMR spectrum of compound **17**, the NH proton signal is shifted to a weak field compared with that for 1,4-dihydropyridines **13a**–**13h** and appears as a broadened singlet in the region of 12.49 ppm. In a series of functionally substituted 2-allylthio(seleno)-1,4-dihydropyridines [3,3] sigmatropic rearrangement has been first reported by us earlier [19].

Spectral characteristics of the synthesized compounds **5–7**, **9–11**, **13–16** confirm their structure. In the ^1H NMR spectra of substituted 1,4-dihydropyridines **5a**, **5b**, **10a**, **10b**, **13a**, **13h**, **15a**, and **15d** there are characteristic proton signals of the dihydropyridine ring in the regions of 4.64–5.18 (C^4H) and 8.91–11.95 (N^1H) ppm disappearing in the spectra of pyridines **14a**–**14c**. We note the splitting of proton signals of the SCH_2 group into two doublets at 3.58–3.94 and 3.75–3.99 ppm (^2J = 14.8–16.7 Hz), which indicates the absence of free rotation of substituent Z. In the spectra of 1,4-dihydropyridine derivatives **13a** and **13b**, the protons of the methyl groups of the isopropyl substituent appear as two doublets in the ranges of 0.99–1.13 and 1.08–1.24 ppm, which also indicates the absence of free rotation around the C^2_{Py}–$CH(Me)_2$ bond. As a result, the protons of the methyl groups are magnetically nonequivalent.

In the ^1H NMR spectrum of compound **13f**, doubling of the H^4 and NH proton signals of the 1,4-dihydropyridine moiety is observed in the form of singlets at 4.68 and 4.71 ppm, 10.02 and 10.16 ppm, respectively, which is probably due to different conformation 1,4-dihydropyridine ring.

In conclusion, multicomponent condensation of malononitrile, hydrogen sulfide, aryl or hetaryl aldehydes, 1,3-dicarbonyl compounds and alkylating reagents is a convenient method for the synthesis of functionalized nitriles and esters of 6-alkylsulfanyl-1,4-dihydronicotinic acid, as well as their aromatic analogues, such as thiazolo[2,3-*b*]pyridine and 1,4-dihydrothieno[2,3-*b*]-pyridines.

EXPERIMENTAL

IR spectra were recorded on an IKS-40 instrument from liquid paraffin. ^1H and ^{13}C NMR spectra were recorded on a Varian VXR-400 spectrometer (399.97 and 100 MHz, respectively) from DMSO-d_6 solutions, and the internal standard was TMS. Mass spectra were registered on an Agilent 1100 Series spectrometer with an Agilent LS/MSDLS selective detector (the sample was introduced into a CH_3COOH matrix, EI, 70 eV). For compounds **10a** and **15b**, mass spectra were taken on an Orbitrap Elite high-resolution mass spectrometer. Elemental analysis was performed on a PerkinElmer CHN-analyzer. Melting points were determined on a Kofler instrument. The reaction progress and the purity of the obtained compounds were monitored by TLC on Silufol UV-254 plates in an acetone–hexane system (3 : 5), developing with iodine vapor and UV irradiation.

Triethylammonium 6-propyl-4-(furan-2-yl)-3-cyano-5-ethoxycarbonyl-1,4-dihydropyridine-2-thiolate (5a). A solution of 0.7 g (10 mmol) of malononitrile **1** and 3 drops of triethylamine in 50 mL of ethanol at 20°C was bubbled with a moderate flow of hydrogen sulfide for 1 h before the start of crystallization of cyanothioacetamide **A**, after which bubbling was stopped. Then, 0.83 mL (10 mmol) of furfural **3a** was added to the mixture. The resulting mixture was stirred for 30 min until crystallization of 2-furfurylidene cyanothioacetamide **B** started. Next, 1.6 mL (10 mmol) of ethyl butylacetate **4a** and 1.4 mL (10 mmol) of triethylamine were successively added. The resulting mixture was stirred for 15 min and kept for 2 days. The precipitate formed was filtered off, washed with ethanol and hexane. Yield 3.9 g (71%), yellow crystalline powder, mp 96–98°C. IR spectrum, ν, cm^{-1}: 3212, 2960 (NH), 2179 (C≡N), 1683 (C=O). ^1H NMR spectrum, δ, ppm: 0.87 t (3H, Me, J = 6.9 Hz), 1.08 t (3H, **Me**CH_2O, J = 7.0 Hz), 1.6 t (9H, Me, J = 7.3 Hz), 1.33–1.59 m (2H, CH_2), 2.61 t (2H, CH_2, J = 7.0 Hz), 3.08 q [6H, (Me**C**H_2)$_3N^+$, J = 7.3 Hz], 3.94 q (2H, CH_2O, J = 6.9 Hz), 4.39 s (1H, H^4_{Py}), 5.74 d (1H, H^3_{Fu}, J = 2.9 Hz), 6.23 d. d (1H, H^4_{Fu}, J = 4.6 Hz), 7.40 d (1H, H^5_{Fu}, J = 1.2 Hz), 8.23 br. s (1H, NH). The signals of HN^+ protons do not appear, apparently, due to fast deutero exchange. Mass spectrum, m/z (I_{rel}, %): 102.2 (10) [Et_3NH + 1]$^+$ 319.0 (100) [M_{anion} + 1]$^+$. Found, %: C 62.85; H 7.84; N 9.96. $C_{22}H_{33}N_3O_3S$. Calculated, %: C 62.98; H 7.93; N 10.02. M 419.6.

Morpholin-4-ium 5-acetyl-6-methyl-4-(5-methylfuran-2-yl)-3-cyano-1,4-dihydropyridine-

2-thiolate (5b) was prepared similarly from 1 mL (10 mmol) of 5-methylfurfural **3b**, 1.23 mL (10 mmol) of acetylacetone **4c** and 0.87 mL (10 mmol) of morpholine. Yield 2.8 g (77%), colorless powder, mp 118–120°C. IR spectrum, ν, cm^{-1}: 3316 (NH), 2170 (C≡N), 1714 (C=O). ^1H NMR spectrum, δ, ppm: 2.11 s (3H, Me), 2.43 s (3H, Me), 2.52 s (3H, Me), 3.08 t (4H, $CH_2N^+CH_2$, J = 4.4 Hz), 3.74 t (4H, CH_2OCH_2, J = 4.4 Hz), 4.36 s (1H, H^4_{Py}), 5.68 d (1H, H^3_{Fu}, J = 2.9 Hz), 5.88 d (1H, H^4_{Fu}, J = 2.9 Hz), 8.31 br. s (1H, NH). The signals of H_2N^+ protons do not appear, apparently, due to fast deutero exchange. Mass spectrum, *m/z* (I_{rel}, %): 274.0 (100) $[M_{anion} + 1]^+$. Found, %: C 59.72; H 6.35; N 11.52. $C_{18}H_{23}N_3O_3S$. Calculated, %: C 59.81; H 6.41; N 11.63. *M* 361.5.

Ethyl 2-methyl-4-(3-methylthiophen-2-yl)-6-thioxo-5-cyano-1,4,5,6-tetrahydropyridine-3-carboxylate (6) was prepared similarly from 1.1 mL (10 mmol) of 3-methylthiophen-2-ylcarbaldehyde **3c** and 1.3 mL (10 mmol) of acetoacetate **4b**. Before filtration, the reaction mixture was diluted with 10% hydrochloric acid to pH = 5 and kept for a day. The precipitate formed was filtered off, washed successively with water, ethanol and hexane. Yield 2.2 g (68%), yellow powder, mp 135–137°C (EtOH). IR spectrum, ν, cm^{-1}: 3335 (NH), 2247 (C≡N), 1711 (C=O), 1188 (C=S). ^1H NMR spectrum, δ, ppm: 1.20 t (3H, **Me**CH_2, J = 7.0 Hz), 2.31 s (3H, Me), 2.36 s (3H, Me), 4.11 q (2H, CH_2O, J = 7.0 Hz), 4.29–4.44 m (2H, H^3_{Py} + H^4_{Py}), 6.76 d (1H, $H^4_{thiophene}$, J = 5.2 Hz), 7.11 d (1H, $H^5_{thiophene}$, J = 5.2 Hz), 12.08 br. s (1H, NH). Mass spectrum, *m/z* (I_{rel}, %): 321.0 (100) $[M + 1]^+$. Found, %: C 56.02; H 4.96; N 8.66. $C_{15}H_{16}N_2O_2S_2$. Calculated, %: C 56.23; H 5.03; N 8.74. *M* 320.4.

Ethyl 2-propyl-6-thioxo-4-(furan-2-yl)-5-cyano-1,6-dihydropyridine-3-carboxylate (7) was obtained by recrystallization of 1 g (2.4 mmol) of salt **5a** from 25 mL of glacial acetic acid. Yield 2.4 g (75%), yellow crystals, mp 183–185°C (AcOH). IR spectrum, ν, cm^{-1}: 3157 (NH), 2223 (C≡N), 1724 (C=O), 1029 (C=S). ^1H NMR spectrum, δ, ppm: 0.88 t (3H, **Me**CH_2O, J = 7.3 Hz), 1.09 t (3H, Me, J = 7.0 Hz), 1.51–1.56 m (2H, CH_2), 2.67 t (2H, CH_2, J = 7.0 Hz), 4.14 q (2H, CH_2O, J = 7.3 Hz), 6.80 s (1H, H^3_{Fu}), 7.38 s (1H, H^4_{Fu}), 8.03 s (1H, H^5_{Fu}), 14.24 br. s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 13.60, 13.83, 22.95, 32.78, 61.92, 109.74, 113.03, 115.58, 116.30, 117.16, 140.85, 145.88, 147.25, 155.83, 164.96, 179.10. Mass spectrum, *m/z* (I_{rel}, %): 315.0 (100) $[M + 1]^+$. Found, %: C 61.01; H 5.10; N 8.84. $C_{16}H_{16}N_2O_3S$. Calculated, %: C 61.13; H 5.13; N 8.91. *M* 314.4.

Ethyl 5-propyl-7-(furan-2-yl)-8-cyano-3,7-dihydro-2*H*-thiazolo[3,2-*a*]pyridine-6-carboxylate (9) was prepared from salt **5a**. The formed salt **5a** was filtered off and dissolved in 25 mL of DMF. To the prepared solution 0.9 mL (10 mmol) of 1,2-dibromoethane **8** and 5.6 mL (10 mmol) of a 10% aqueous KOH solution were successively added. The resulting mixture was stirred for 1 h and kept for 2 days, then diluted with an equal volume of water. The precipitate formed was filtered off, washed with water, ethanol and hexane. Yield 2.7 g (78%), colorless powder, mp 112–114°C (EtOH). IR spectrum, ν, cm^{-1}: 2191 (C≡N), 1694 (C=O). ^1H NMR spectrum, δ, ppm: 0.94 t (3H, Me, J = 7.2 Hz), 1.11 t (3H, Me, J = 7.1 Hz), 1.39–1.64 m (2H, CH_2), 2.58–2.77 m (1H, CH_2), 2.79–2.92 m (1H, CH_2), 3.42 t (2H, CH_2, J = 7.4 Hz), 4.05 q (2H, CH_2O, J = 7.2 Hz), 4.08–4.12 m (1H, CH_2), 4.19–4.26 m (1H, CH_2), 4.74 s (1H, H^7_{Py}), 6.02 d (1H, H^3_{Fu}, J = 2.9 Hz), 6.35 s (1H, H^4_{Fu}), 7.53 s (1H, H^5_{Fu}). ^{13}C NMR spectrum, δ_C, ppm: 13.77, 14.00, 21.53, 28.27, 31.21, 35.13, 51.95, 59.83, 74.84, 100.76, 105.39, 110.61, 119.52, 142.39, 149.79, 153.74, 156.74, 166.14. Mass spectrum, *m/z* (I_{rel}, %): 345.2 (100) $[M + 1]^+$. Found, %: C 62.61; H 5.70; N 7.97. $C_{18}H_{20}N_2O_3S$. Calculated, %: C 62.77; H 5.85; N 8.13. *M* 344.4.

Diethyl 6,6'-[ethane-1,2-diylbis(sulfanediyl)]-bis[5-cyano-2-methyl-4-(3-methylyhiophen-2-yl)-1,4-dihydropyridine-3-carboxylate] (10a) was prepared similarly to compound **9** from 1.1 mL (10 mmol) of 3-methylthiophen-2-ylcarbaldehyde **3c** and 0.45 mL (5 mmol) of 1,2-dibromoethane **8**. Yield 2.3 g (68%), yellow powder, mp 263–265°C (BuOH). IR spectrum, ν, cm^{-1}: 3330 (NH), 2198 (C≡N), 1716 (C=O). ^1H NMR spectrum, δ, ppm: 1.06 t (6H, Me, J = 7.1 Hz), 2.18 s (6H, Me), 2.21 s (6H, Me), 2.98 t (2H, CH_2, J = 7.3 Hz), 3.14 t (2H, CH_2, J = 7.3 Hz), 3.95 q (4H, CH_2O, J = 7.1 Hz), 4.89 s (2H, H^4_{Py}), 6.75 d (2H, $H^4_{thiophene}$, J = 5.1 Hz), 7.19 d (2H, $H^5_{thiophene}$, J = 5.1 Hz), 9.65 br. s (2H, NH). ^{13}C NMR spectrum, δ_C, ppm: 13.73 (2C), 14.42 (2C), 18.11 (2C), 32.76 (2C), 35.75 (2C), 59.96 (2C), 92.51 (2C), 101.17 (2C), 119.50 (2C), 123.92 (2C), 130.25 (2C), 132.35 (2C), 141.14 (2C), 144.46 (2C), 145.93 (2C), 166.36 (2C). Mass spectrum, *m/z*: 665.1392 $[M - H]^+$ (calculated for $C_{32}H_{34}N_4O_4S_4$: 665.1463).

Diethyl 6,6'-[ethane-1,2-diethylbis(sulfandiyl)]-bis[4-(2-methoxyphenyl)-2-phenyl-5-cyano-1,4-dihydropyridine-3-carboxylate] (10b) was prepared

similarly to compound **9** from 1.21 mL (10 mmol) *o*-methoxybenzaldehyde **3d**, 1.73 mL (10 mmol) of ethylbenzoylacetate **4d** and 0.45 mL (5 mmol) of 1,2-dibromoethane **8**. Yield 2.8 g (70%), yellow crystals, mp 225–227°C (*i*-PrOH). IR spectrum, ν, cm^{-1}: 3311 (NH), 2202 (C≡N), 1707 (C=O). ^1H NMR spectrum, δ, ppm: 0.68 t (6H, Me, *J* = 7.0 Hz), 2.91–3.02 m (2H, CH_2), 3.24–3.29 m (2H, CH_2), 3.65 q (4H, CH_2O, *J* = 7.0 Hz), 3.76 s (6H, MeO), 4.97 s (2H, H^4_{Py}), 6.93 t (2H, H_{Ar}, *J* = 7.4 Hz), 7.02 d (2H, H_{Ar}, *J* = 8.2 Hz), 7.20 d (3H, H_{Ar}, *J* = 7.4 Hz), 7.23 t (2H, H_{Ar}, *J* = 7.8 Hz), 7.34 d (4H, H_{Ar}, *J* = 7.0 Hz), 7.38–7.47 m (5H, H_{Ar}), 9.86 br. s (2H, NH). ^{13}C NMR spectrum, δ_C, ppm: 13.77 (2C), 32.43 (2C), 36.72 (2C), 55.88 (2C), 59.62 (2C), 90.23 (2C), 100.40 (2C), 111.81 (2C), 119.43 (2C), 121.07 (2C), 128.40 (4C), 128.49 (2C), 128.88 (2C), 129.24 (4C), 129.50 (2C), 132.77 (2C), 136.10 (2C), 143.09 (2C), 148.06 (2C), 156.73 (2C), 166.31 (2C). Mass spectrum, *m/z* (I_{rel}, %): 811.2 (100) $[M + 1]^+$. Found, %: C 68.02; H 5.14; N 6.78. $C_{46}H_{42}N_4O_6S_2$. Calculated, %: C 68.13; H 5.22; N 6.91. *M* 810.991.

Diethyl 6,6'-[ethane-1,2-diylbis(sulfanediyl)]-bis[2-propyl-4-(furan-2-yl)-5-cyanonicotinate] (11) was prepared similarly to compound **9** from 0.45 mL (5 mmol) of 1,2-dibromoethane. Yield 2.2 g (66%), colorless powder, mp 148–150°C (AcOH). IR spectrum, ν, cm^{-1}: 2222 (C≡N), 1739 (C=O). ^1H NMR spectrum, δ, ppm: 0.88 t (6H, Me, *J* = 7.2 Hz), 1.18 t (6H, **Me**CH_2O, *J* = 7.3 Hz), 1.57–1.76 m (4H, CH_2), 2.69 t (4H, SCH_2, *J* = 7.0 Hz), 3.72 t (4H, CH_2, *J* = 7.3 Hz), 4.28 q (4H, CH_2O, *J* = 7.3 Hz), 6.77 s (2H, H^3_{Fu}), 7.25 s (2H, H^4_{Fu}), 7.99 s (2H, H^5_{Fu}). ^{13}C NMR spectrum, δ_C, ppm: 13.64 (2C), 13.88 (2C), 21.36 (2C), 29.82 (2C), 37.39 (2C), 61.95 (2C), 100.01 (2C), 112.91 (2C), 115.03 (2C), 115.54 (2C), 122.09 (2C), 138.35 (2C), 145.44 (2C), 146.75 (2C), 161.82 (2C), 163.01 (2C), 166.34 (2C). Mass spectrum, *m/z* (I_{rel}, %): 659.2 (100) $[M + 1]^+$. Found, %: C 61.85; H 5.07; N 8.41. $C_{34}H_{34}N_4O_6S_2$. Calculated, %: C 61.99; H 5.20; N 8.50. *M* 658.8.

Substituted 2-alkylsulfanyl-1,4-dihydropyridines (13a–13h) and pyridines (14a–14c) were obtained analogously to compounds **5** from the corresponding aldehydes **3a**–**3h** and CH acids **4a**–**4f**. After the step of salt **5** precipitate formation, the alkyl halide **12a**–**12h** was added with stirring. The mixture was stirred for 2 h and kept for a day, then diluted with an equal volume of water and again kept for a day. The precipitate formed was filtered off, washed successively with water, ethanol and hexane.

Methyl 2-isopropyl-4-(2-methyl-4-fluorophenyl)-6-[2-(4-chlorophenyl)-2-oxoethylthio)]-5-cyano-1,4-dihydropyridine-3-carboxylate (13a). Yield 4.1 g (82%), yellow crystals, mp 134–136°C (AcOH). IR spectrum, ν, cm^{-1}: 3310 (NH), 2200 (C≡N), 1719 (OC=O), 1698 (C=O). ^1H NMR spectrum, δ, ppm: 1.09 d (3H, **Me**CH, *J* = 6.8 Hz), 1.23 d (3H, **Me**CH, *J* = 6.8 Hz), 2.40 s (3H, Me), 3.48 s (3H, MeO), 4.01–4.18 m (1H, **CH**Me_2), 4.70 s (2H, CH_2), 4.78 s (1H, H^4_{Py}), 6.82–6.95 m (2H, H_{Ar}), 7.02–7.05 m (1H, H_{Ar}), 7.61 d (2H, H_{Ar}, *J* = 8.4 Hz), 7.99 d (2H, H_{Ar}, *J* = 8.4 Hz), 8.92 br. s (1H, NH). Mass spectrum, *m/z* (I_{rel}, %): 500.2 (100) $[M + 1]^+$. Found, %: C 62.41; H 4.77; N 5.58. $C_{26}H_{24}FClN_2O_3S$. Calculated, %: C 62.58; H 4.85; N 5.61. *M* 499.0.

Methyl 6-(2-amino-2-oxoethylthio)-2-isopropyl-4-(2-methyl-4-fluorophenyl)-5-cyano-1,4-dihydropyridine-3-carboxylate (13b). Yield 3.2 g (79%), colorless powder, mp 198–200°C (*i*-PrOH). IR spectrum, ν, cm^{-1}: 3412–3290 (NH, NH_2), 2204 (C≡N), 1719 (C=O), 1666 (CONH). ^1H NMR spectrum, δ, ppm: 1.13 d (3H, **Me**CH, *J* = 6.6 Hz), 1.24 d (3H, **Me**CH, *J* = 6.6 Hz), 2.42 s (3H, Me), 3.48 s (3H, MeO), 3.58 d (1H, SCH_2, *J* = 15.5 Hz), 3.75 d (1H, SCH_2, *J* = 15.5 Hz), 4.02–4.19 m (1H, **CH**Me_2), 4.81 s (1H, H^4_{Py}), 6.84–7.01 m (2H, H_{Ar}), 7.03–7.15 m (1H, H_{Ar}), 7.85 br. s (1H, NH_2), 8.14 br. s (1H, NH_2), 10.57 br. s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 19.21, 20.04, 21.44, 28.13, 35.14, 37.45, 51.55, 86.04, 100.50, 114.23, 116.81, 119.48, 130.27, 137.20, 141.64, 144.43, 154.38, 159.84, 167.10, 173.40. Mass spectrum, *m/z* (I_{rel}, %): 404.2 (100) $[M + 1]^+$. Found, %: C 59.44; H 5.39; N 10.32. $C_{20}H_{22}FN_3O_3S$. Calculated, %: C 59.54; H 5.50; N 10.41. *M* 403.5.

Methyl 6-[2-oxo-(2-oxo-2*H*-chromen-3-yl)-ethylthio]-2-isopropyl-4-(2-methyl-4-fluorophenyl)-5-cyano-1,4-dihydropyridine-3-carboxylate (13c). Yield 3.9 g (74%), yellow crystals, mp 250–252°C (dioxane). IR spectrum, ν, cm^{-1}: 3320 (NH), 2205 (C≡N), 1715, 1695 (C=O). ^1H NMR spectrum, δ, ppm: 1.29 d (6H, 2Me, *J* = 6.6 Hz), 2.76 s (3H, Me), 3.56 br. s (5H, MeO + SCH_2), 4.18–4.26 m (1H, **CH**Me_2), 5.37 s (1H, H^4_{Py}), 6.72–6.81 m (2H, H_{Ar}), 7.10 br. s (1H, H_{Ar}), 7.24–7.33 m (2H, H_{Ar}), 7.49 br. s (1H, H_{Ar}), 8.24 br. s (1H, H_{Ar}), 9.85 s (1H, $H^4_{coumarin}$), 11.68 br. s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 20.09 (2C), 20.63, 22.80, 28.32, 51.16, 66.81, 86.13, 87.12, 103.01, 113.25, 116.03, 117.14, 119.02, 124.86, 125.07, 132.16, 133.04, 137.09, 143.98, 147.12,

150.96, 152.17, 153.10, 158.96, 161.12, 162.15, 165.05, 168.17. Mass spectrum, *m/z* (I_{rel}, %): 533.0 (100) [M + 1]$^+$. Found, %: C 65.37; H 4.68; N 5.22. $C_{29}H_{25}FN_2O_5S$. Calculated, %: C 65.40; H 4.73; N 5.30. M 532.6.

Allyl 6-{[2-oxo-(*o*-tolylamino)ethyl]thio}2-propyl-4-furan-2-yl-5-cyano-1,4-dihydropyridine-3-carboxylate (13d). Yield 3.8 g (84%), colorless powder, under UV irradiation fluoresces, mp 160–162°C (BuOH). IR spectrum, ν, cm^{-1}: 3380–3295 (NH), 2196 (C≡N), 1715 (C=O), 1668 (NHCO). ^{1}H NMR spectrum, δ, ppm: 2.20 s (3H, Me), 2.31 s (3H, Me), 3.94 d (1H, SCH_2, J = 14.8 Hz), 3.99 d (1H, SCH_2, J = 14.8 Hz), 3.91–4.62 m (2H, OCH_2), 4.69 s (1H, H^4_{Py}), 5.13 d (1H, CH_2=, J_{cis} = 9.2 Hz), 5.17 d (1H, CH_2=, J_{trans} = 15.9 Hz), 5.77–5.98 m (1H, =CH), 6.05 d (1H, H^3_{Fu}, J = 3.0 Hz), 6.34 t (1H, H^4_{Fu}, J = 1.8 Hz), 7.08 t (1H, H_{Ar}, J = 8.2 Hz), 7.10 t (1H, H_{Ar}, J = 8.0 Hz), 7.13 d (1H, H_{Ar}, J = 8.2 Hz), 7.32 d (1H, H_{Ar}, J = 7.8 Hz), 7.52 s (1H, H^5_{Fu}), 9.80 br. s (1H, NH), 10.15 br. s (1H, CONH). ^{13}C NMR spectrum, δ_C, ppm: 18.18, 18.26, 36.02, 36.38, 64.54, 85.41, 97.85, 105.99, 111.05, 119.31, 119.94, 125.60, 126.35, 126.58, 130.90, 132.53, 135.94, 136.59, 142.92, 144.87, 147.70, 156.47, 166.05, 167.94. Mass spectrum, *m/z* (I_{rel}, %): 448.0 (100) [M – 1]$^+$. Found, %: C 64.02; H 5.04; N 9.19. $C_{24}H_{23}N_3O_4S$. Calculated, %: C 64.13; H 5.16; N 9.35. M 449.5.

Ethyl 4-(2-methoxyphenyl)-6-[(3-methyl-1-oxo-1-phenylbut-2-yl)thio]-2-phenyl-5-cyano-1,4-dihydropyridine-3-carboxylate (13e). Yield 4.8 g (86%), yellow powder, mp 156–158°C (EtOH). IR spectrum, ν, cm^{-1}: 3306 (NH), 2222 (C≡N), 1714, 1698 (C=O). ^{1}H NMR spectrum, δ, ppm: 0.76 t (3H, Me, J = 7.0 Hz), 0.99 d (3H, Me, J = 6.5 Hz), 1.08 d (3H, Me, J = 6.5 Hz), 2.19–2.25 m (1H, **CH**Me_2), 3.66 q (2H, CH_2O, J = 7.0 Hz), 3.85 s (3H, MeO), 4.94 s (1H, H^4_{Py}), 5.07 d (1H, SCH, J = 7.0 Hz), 6.81–6.92 m (2H, H_{Ar}), 7.10–7.18 m (2H, H_{Ar}), 7.23 d (2H, H_{Ar}, J = 7.5 Hz), 7.34 t (2H, H_{Ar}, J = 7.5 Hz), 7.38 d (1H, H_{Ar}, J = 7.0 Hz), 7.47 d (2H, H_{Ar}, J = 7.5 Hz), 7.61 t (1H, H_{Ar}, J = 7.0 Hz), 7.95 d (2H, H_{Ar}, J = 7.5 Hz), 9.35 br. s (1H, NH). Mass spectrum, *m/z* (I_{rel}, %): 551.2 (100) [M – 1]$^+$. Found, %: C 71.65; H 5.72; N 4.96. $C_{33}H_{32}N_2O_4S$. Calculated, %: C 71.72; H 5.84; N 5.07. M 552.7.

Ethyl 2'-phenyl-5'-cyano-6'-(cyclohex-2-en-1-ylthio)-1',4'-dihydro-(3,4'-bipyridine)-3'-carboxylate (13f). Yield 3.5 g (78%), pale yellow crystals, under UV irradiation fluoresces, mp 165–167°C (EtOH). IR spectrum, ν, cm^{-1}: 3318 (NH), 2205 (C≡N), 1719 (C=O). ^{1}H NMR spectrum, δ, ppm: 0.71 t (3H, Me, J = 7.2 Hz), 1.49–2.18 m (6H, H_{Cy}), 3.71 q (2H, CH_2O, J = 7.2 Hz), 4.22–4.29 m (1H, SCH), 4.68 s and 4.71 s (1H, H^4_{Py}), 5.15–5.23 m (1H, =CH), 5.28–6.01 m (1H, CH=), 7.32 d (2H, H_{Ar}, J = 6.8 Hz), 7.38–7.53 m (4H, H_{Ar}), 7.71 q (1H, H_{Ar}, J = 8.0 Hz), 8.50 s (1H, H^2_{Py}), 8.54 d (1H, H^6_{Py}, J = 5.2 Hz), 10.02 br. s and 10.16 br. s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 13.73, 18.05, 19.64, 24.70, 28.22, 43.69, 59.87, 90.55, 91.96, 100.53, 119.33 (2C), 124.71, 126.34, 128.46 (2C), 129.20, 131.57, 140.64, 143.71, 144.32, 147.94, 148.08, 148.56, 148.97, 166.13. Mass spectrum, *m/z* (I_{rel}, %): 444.0 (100) [M + 1]$^+$. Found, %: C 70.29; H 5.54; N 9.33. $C_{26}H_{25}N_3O_2S$. Calculated, %: C 70.40; H 5.68; N 9.47. M 443.6.

5-Acetyl-6-methyl-4-(2-chlorophenyl)-2-(cyclohex-2-en-1-ylthio)-1,4-dihydropyridine-3-carboxylate (13g). Yield 2.9 g (76%), red powder, under UV irradiation fluoresces, mp 157–159°C (EtOH). IR spectrum, ν, cm^{-1}: 3300 (NH), 2202 (C≡N), 1714 (C=O). ^{1}H NMR spectrum, δ, ppm: 1.51–1.72 m (2H, H_{Alk}), 1.76–1.81 m (2H, H_{Alk}), 1.83–1.99 m (2H, H_{Alk}), 2.04 s (3H, Me), 2.37 s (3H, MeCO), 4.18–4.26 m (1H, SCH), 5.18 s (1H, H^4_{Py}), 5.61–5.66 m (1H, =CH), 5.84–5.93 m (1H, =CH), 7.20 d (1H, H_{Ar}, J = 7.7 Hz), 7.23 t (1H, H_{Ar}, J = 7.7 Hz), 7.33 t (1H, H_{Ar}, J = 7.4 Hz), 7.40 d (1H, H_{Ar}, J = 8.0 Hz), 9.72 br. s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 18.20, 19.36, 24.69, 24.85, 28.31, 30.34, 43.90, 92.27, 109.75, 119.01, 124.92, 128.72, 129.37, 129.86, 130.48, 142.70, 142.99, 143.08, 143.12, 146.51, 196.80. Mass spectrum, *m/z* (I_{rel}, %): 385.0 (100) [M + 1]$^+$. Found, %: C 65.48; H 5.44; N 7.16. $C_{21}H_{21}ClN_2OS$. Calculated, %: C 65.60; H 5.50; N 7.29. M 384.5.

Ethyl 4-(pyridin-3-yl)-6-(prop-2-yn-1-ylthio)-2-phenyl-5-cyano-1,4-dihydropyridinenicotinate (13h). Yield 2.8 g (70%), pale yellow crystals, under UV irradiation fluoresces, mp 145–147°C (EtOH). IR spectrum, ν, cm^{-1}: 3333 (NH, ≡C–H), 2244 (C≡C), 2203 (C≡N), 1722 (C=O). ^{1}H NMR spectrum, δ, ppm: 0.77 t (3H, Me, J = 7.2 Hz), 3.02 s (1H, ≡C–H), 3.74 q (2H, OCH_2, J = 7.2 Hz), 3.77 d (1H, SCH_2, J = 16.7 Hz), 4.10 d (1H, SCH_2, J = 16.7 Hz), 4.64 s (1H, H^4_{Py}), 7.26–7.38 m (6H, H_{Ar}), 7.67 d (1H, H_{Ar}, J = 7.2 Hz), 8.43–8.51 m (2H, H_{Ar}), 9.93 br. s (1H, NH). Mass spectrum, *m/z* (I_{rel}, %): 402.0 (100) [M + 1]$^+$. Found, %: C 68.72; H 4.65; N 10.38. $C_{23}H_{19}N_3O_2S$. Calculated, %: C 68.81; H 4.77; N 10.47. M 401.5.

5-Acetyl-6-methyl-4-(5-methylfuran-2-yl)-2-(prop-2-yn-1-ylthio)nicotinonitrile (14a). Yield 2.4 g (77%),

yellow powder, under UV irradiation fluoresces, mp 93–95°C (*i*-PrOH). IR spectrum, ν, cm^{-1}: 3330 (≡C–H), 2222 (C≡N), 2150 (C≡C), 1712 (C=O). ^{1}H NMR spectrum, δ, ppm: 2.25 s (3H, Me), 2.34 s (3H, Me), 2.49 s (3H, Me), 3.18 t (1H, ≡CH, *J* = 2.4 Hz), 4.13 d (2H, CH_2, *J* = 2.4 Hz), 6.45 d (1H, H^4_{Fu}, *J* = 3.4 Hz), 7.24 d (1H, H^3_{Fu}, *J* = 3.4 Hz). ^{13}C NMR spectrum, δ_C, ppm: 13.66, 18.80, 23.54, 31.34, 74.14, 80.01, 98.96, 110.22, 115.65, 117.86, 129.55, 137.28, 143.96, 156.95, 157.85, 161.31, 202.81. Mass spectrum, *m/z* (I_{rel}, %): 311.0 (100) $[M+1]^+$. Found, %: C 65.64; H 4.39; N 10.22. $C_{17}H_{14}N_2O_2S$. Calculated, %: C 65.79; H 4.55; N 10.33. *M* 310.4.

5-Acetyl-2-benzylthio-6-methyl-4-(4-chlorophenyl)-nicotinonitrile (14b). Yield 3.3 g (84%), yellow powder, mp 130–132°C (AcOH). IR spectrum, ν, cm^{-1}: 2225 (C≡N), 1717 (C=O). ^{1}H NMR spectrum, δ, ppm: 1.99 s (3H, Me), 2.54 s (3H, Me), 4.57 s (2H, CH_2), 7.25 d (1H, H_{Ar}, *J* = 6.5 Hz), 7.32 t (2H, H_{Ar}, *J* = 6.5 Hz), 7.41 d (2H, H_{Ar}, *J* = 8.0 Hz), 7.47 d (2H, H_{Ar}, *J* = 7.0 Hz), 7.60 d (2H, H_{Ar}, *J* = 8.0 Hz). Mass spectrum, *m/z* (I_{rel}, %): 393.3 (100) $[M+1]^+$. Found, %: C 67.18; H 4.25; N 7.02. $C_{22}H_{17}ClN_2OS$. Calculated, %: C 67.25; H 4.36; N 7.13. *M* 392.9.

Ethyl 6-[2-oxo-2-(2-oxo-2*H*-chromen-3-yl)ethylthio]-2-propyl-4-(furan-2-yl)-5-cyanonicotinate (14c). Yield 3.6 g (71%), colorless powder, mp 180–182°C (BuOH). IR spectrum, ν, cm^{-1}: 2227 (C≡N), 1733 (C=O). ^{1}H NMR spectrum, δ, ppm: 0.66 t (3H, Me, *J* = 7.2 Hz), 1.17 t (3H, Me, *J* = 7.3 Hz), 1.38–1.62 m (2H, CH_2), 2.56 t (2H, CH_2, *J* = 7.3 Hz), 4.26 q (2H, CH_2O, *J* = 7.2 Hz), 4.89 s (2H, SCH_2), 6.78 d. d (1H, H^4_{Fu}, *J* = 1.7, 3.5 Hz), 7.26 d (1H, H^3_{Fu}, *J* = 3.5 Hz), 7.43 t (1H, H_{Ar}, *J* = 6.7 Hz), 7.50 d (1H, H_{Ar}, *J* = 8.3 Hz), 7.79 t (1H, H_{Ar}, *J* = 8.3 Hz), 7.98 br. s (2H, H^5_{Fu} + H_{Ar}), 8.77 s (1H, $H^4_{coumarin}$). ^{13}C NMR spectrum, δ_C, ppm: 13.46, 13.87, 21.52, 24.48, 37.33, 61.98, 99.39, 112.95, 115.14, 115.65, 116.30, 118.15, 121.89, 123.63, 125.28, 131.06, 135.10, 138.17, 145.36, 146.79, 148.44, 154.74, 158.61, 161.72, 162.78, 166.29, 190.66. Mass spectrum, *m/z* (I_{rel}, %): 503.2 (100) $[M+1]^+$. Found, %: C 64.41; H 4.38; N 5.45. $C_{27}H_{22}N_2O_6S$. Calculated, %: C 64.53; H 4.41; N 5.57. *M* 502.5.

Substituted 4,7-dihydrothieno[2,3-*b*]pyridines (15a–15d) were obtained similarly to compounds **5**. After the precipitate formation, to the mixture 10 mmol of the corresponding alkylating agent **12b, 12i** or **12j** was added. The resulting mixture was stirred for 2 h, diluted with 20 mL of DMF, and 5.6 mL (10 mmol) of a 10% aqueous solution of KOH was added. The mixture was stirred for 2 h. Next day, the mixture was diluted with an equal volume of water. The precipitate formed was filtered off and washed with water, ethanol and hexane.

Ethyl 3-amino-2-carbamoyl-4-(pyridin-3-yl)-6-phenyl-4,7-dihydrothieno[2,3-*b*]pyridine-5-carboxylate (15a). Yield 3.0 g (72%), pale yellow powder, mp 190–192°C (PrOH). IR spectrum, ν, cm^{-1}: 3400–3295 (NH, NH_2), 1722 (C=O), 1668 ($CONH_2$), 1635 [δ(NH_2)]. ^{1}H NMR spectrum, δ, ppm: 0.69 t (3H, Me, *J* = 6.4 Hz), 3.66 q (2H, OCH_2, *J* = 6.4 Hz), 5.17 s (1H, $H^4_{dihydropyridine}$), 6.46 br. s (2H, NH_2), 6.57 br. s (2H, NH_2), 7.24–7.49 m (6H, H_{Ar}), 7.72 d (1H, H_{Ar}, *J* = 6.8 Hz), 8.27 br. s (1H, H_{Ar}), 8.64 s (1H, H^2_{Py}), 10.03 br. s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 13.84, 36.78, 59.25, 91.43, 99.87, 111.19, 124.04, 128.38 (2C), 128.70 (2C), 129.13, 135.37, 137.47, 139.56, 142.56, 147.81, 149.17, 149.21, 150.73, 167.05, 167.19. Mass spectrum, *m/z* (I_{rel}, %): 421.0 (100) $[M+1]^+$. Found, %: C 62.70; H 4.68; N 13.25. $C_{22}H_{20}N_4O_3S$. Calculated, %: C 62.84; H 4.79; N 13.32. *M* 420.5.

Ethyl 3-amino-2-carbamoyl-6-methyl-4-(3-methylthiophen-2-yl)-4,7-dihydrothieno[2,3-*b*]-pyridine-5-carboxylate (15b). Yield 2.9 g (77%), yellow crystals, mp 225–227°C (BuOH). IR spectrum, ν, cm^{-1}: 3400–3011 (NH, NH_2), 1718 (OC=O), 1665 ($CONH_2$), 1635 [δ(NH_2)]. ^{1}H NMR spectrum, δ, ppm: 1.11 t (3H, Me, *J* = 7.1 Hz), 2.18 s (3H, Me), 2.23 s (3H, Me), 3.99 q (2H, CH_2, *J* = 7.1 Hz), 5.25 s (1H, H^4_{Py}), 5.91 br. s (2H, C^3NH_2), 6.56 br. s (2H, $CONH_2$), 6.61 d (1H, $H^4_{thiophene}$, *J* = 5.1 Hz), 7.08 d (1H, $H^5_{thiophene}$, *J* = 5.1 Hz), 9.86 br. s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 14.12, 14.68, 19.69, 32.44, 59.37, 91.39, 99.61, 111.95, 122.95, 129.92, 131.94, 138.86, 145.52, 146.62, 150.93, 167.05, 167.37. Mass spectrum, *m/z* 378.0941 $[M+H]^+$ (calculated for $C_{17}H_{19}N_3O_3S_2$: 378.0878).

3-Amino-2-benzyl-4-(pyridin-3-yl)-6-phenyl-5-ethyl-4,7-dihydrothieno[2,3-*b*]pyridine-2,5-carboxylate (15c). Yield 3.8 g (74%), yellow crystals, mp 282–284°C (BuOH). IR spectrum, ν, cm^{-1}: 3400–3312 (NH, NH_2), 1724, 1716 (C=O), 1645 [δ(NH_2)]. ^{1}H NMR spectrum, δ, ppm: 0.65 t (3H, Me, *J* = 7.1 Hz), 3.62 q (2H, Me**C**H_2, *J* = 7.1 Hz), 5.09 d (1H, **C**H_2Ph, *J* = 12.8 Hz), 5.12 d (1H, **C**H_2Ph, *J* = 12.8 Hz), 5.20 s (1H, $H^4_{thienopyridine}$), 6.49 br. s (2H, NH_2), 7.23–7.46 m (11H, H_{Ar}), 7.68 d (1H, H^4_{Py}, *J* = 6.0 Hz), 8.34 d (1H, H^6_{Py}, *J* = 1.6 Hz), 8.61 s (1H, H^2_{Py}), 10.11 br. s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 13.79, 36.48, 59.36, 64.66, 100.66,

109.68, 110.34, 124.10, 128.02, 128.23 (2C), 128.40, 128.61 (2C), 128.85 (4C), 129.18, 135.34, 137.17, 137.47, 142.12, 143.43, 147.93, 148.62, 149.14, 163.86, 166.82. Mass spectrum, *m/z* 512.1647 $[M + 1]^+$ (calculated for $C_{29}H_{25}N_3O_4S$: 512.1566).

Allyl 3-amino-6-propyl-2-(thiazol-2-ylcarbamoyl)-4-(furan-2-yl)-4,7-dihydrothieno[2,3-*b*]pyridine-2,5-carboxylate (15d). Yield 3.5 g (81%), pale yellow crystals, under UV irradiation fluoresces, mp 223–225°C (BuOH). IR spectrum, ν, cm^{-1}: 3400–3296 (NH, NH_2), 1713 (C=O), 1666 (NHCO), 1644 [δ(NH_2)]. ^{1}H NMR spectrum, δ, ppm: 2.87 s (3H, Me), 4.36–4.61 m (2H, CH_2O), 5.11 d (1H, CH_2=, J_{cis} = 10.6 Hz), 5.18 d (1H, CH_2=, J_{trans} = 17.3 Hz), 5.23 s (1H, $H^4_{thienopyridine}$), 5.76–5.84 m (1H, =CH), 5.85 d (1H, H^3_{Fu}, *J* = 2.9 Hz), 6.25 br. s (1H, H^4_{Fu}), 6.77 br. s (3H, NH_2 + $H^5_{thiazole}$), 6.98 d (1H, $H^4_{thiazole}$, *J* = 3.5 Hz), 7.34 d (1H, H^5_{Fu}, *J* = 1.2 Hz), 7.38 br. s (1H, N^7H), 10.06 br. s (1H, CONH). ^{13}C NMR spectrum, δ_C, ppm: 19.83, 32.40, 64.00, 97.15, 103.02, 105.02, 107.11, 110.12, 117.23, 119.16, 122.11, 124.45, 133.98, 142.16, 143.07, 146.16, 148.81, 158.96, 167.05. Mass spectrum, *m/z* (I_{rel}, %): 431.1 (100) $[M + 1]^+$. Found, %: C 52.91; H 4.07; N 12.88. $C_{19}H_{18}N_4O_4S_2$. Calculated, %: C 53.01; H 4.22; N 13.01. *M* 430.5.

5-Acetyl-1-benzyl-6-methyl-2-methylthio-4-phenyl-1,4-dihydronicotinonitrile (16) was obtained similarly to compounds **5.** After the precipitate formation, to the mixture 0.62 mL (10 mmol) of methyl iodide **12k** was added. The mixture was stirred for 2 h, after which 20 mL of DMF, 5.6 mL (10 mmol) of a 10% aqueous solution of KOH and 1.15 mL (10 mmol) of benzyl chloride **12h** were successively added. The mixture was stirred for 1 h and kept for a day, then diluted with an equal volume of water. The precipitate formed was filtered off, washed with water, ethanol and hexane. Yield 2.9 g (77%), yellow powder, mp 172–173°C (EtOH). IR spectrum, ν, cm^{-1}: 2210 (C≡N), 1698 (C=O). ^{1}H NMR spectrum, δ, ppm: 2.16 s (3H, Me), 2.38 s (3H, Me), 2.49 s (3H, SMe), 3.07 d (1H, CH_2, *J* = 13.5 Hz), 3.22 d (1H, CH_2, *J* = 13.5 Hz), 4.13 s (1H, H^4_{Py}), 6.96 d (2H, Ph, *J* = 7.0 Hz), 7.18 d (2H, Ph, *J* = 7.0 Hz), 7.21–7.25 m (3H, Ph), 7.32–7.45 m (3H, Ph). Mass spectrum, *m/z* (I_{rel}, %): 375.2 (100) $[M + 1]^+$. Found, %: C 73.68; H 5.81; N 7.44. $C_{22}H_{22}N_2OS$. Calculated, %: C 73.76; H 5.92; N 7.50. *M* 374.5.

Ethyl 5'-allyl-6'-thioxo-2'-phenyl-5'-cyano-1',4',5',6'-tatrahydro-(3,4'-bipyridine)-3'-carboxylate (17) obtained similarly to compounds **5**. After the precipitate formation, 0.85 mL (10 mmol) of allyl bromide **12l** was added. The mixture was stirred for 2 h and kept for 2 days, then diluted with an equal volume of water. The precipitate formed was filtered off, washed with water, ethanol and hexane. Yield 2.7 g (68%), pale yellow crystals, under UV irradiation fluoresces, mp 125–127°C (EtOH). IR spectrum, ν, cm^{-1}: 3060 (NH), 2244 (C≡N), 1699 (C=O), 1229 (C=S). ^{1}H NMR spectrum, δ, ppm: 0.72 t (3H, Me, *J* = 7.1 Hz), 2.73–2.99 m (2H, CH_2), 3.75 q (2H, OCH_2, *J* = 7.1 Hz), 4.31 s (1H, $H^4_{dihydropyridine}$), 5.31 d (1H, =CH_2, J_{trans} = 17.1 Hz), 5.35 d (1H, =CH_2, J_{cis} = 10.4 Hz), 5.42–6.06 m (1H, CH=), 7.46 br. s (6H, H_{Ar}), 7.65 d (1H, H_{Ar}, *J* = 8.0 Hz), 8.51 s (1H, H^2_{Py}), 8.53 d (1H, H^6_{Py}, *J* = 8.0 Hz), 12.49 br. s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 13.70, 41.22, 43.34, 59.36, 60.60, 108.61, 118.11, 122.11, 124.47, 128.43, 129.04 (2C), 129.91 (2C), 131.15, 133.87, 133.98, 136.02, 145.55, 149.87, 150.02, 165.56, 194.51. Mass spectrum, *m/z* (I_{rel}, %): 404.1 (100) $[M + 1]^+$. Found, %: C 68.32; H 5.11; N 10.35. $C_{23}H_{21}N_3O_2S$. Calculated, %: C 68.46; H 5.25; N 10.41. *M* 403.5.

CONFLICT OF INTEREST

No conflict of interest was declared by the authors.

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