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New Synthetic Approach to Substituted 2-Alkylsulfanyl-4,6-diaryl(heteryl)-1,4-dihydropyridine-, Pyridine-, and Thieno[2,3-*b*]pyridine-3-carbonitriles

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Abstract—Reactions of 1,3-diaryl(heteryl)prop-2-ene-1-thiones with 2-cyanoethanethio(seleno)-amides and alkyl halides led to the formation of substituted 2-alkylsulfanyl-4,6-diaryl(heteryl)-1,4-dihydropyridine-, pyridine-, and thieno[2,3-*b*]pyridine-3-carbonitriles.

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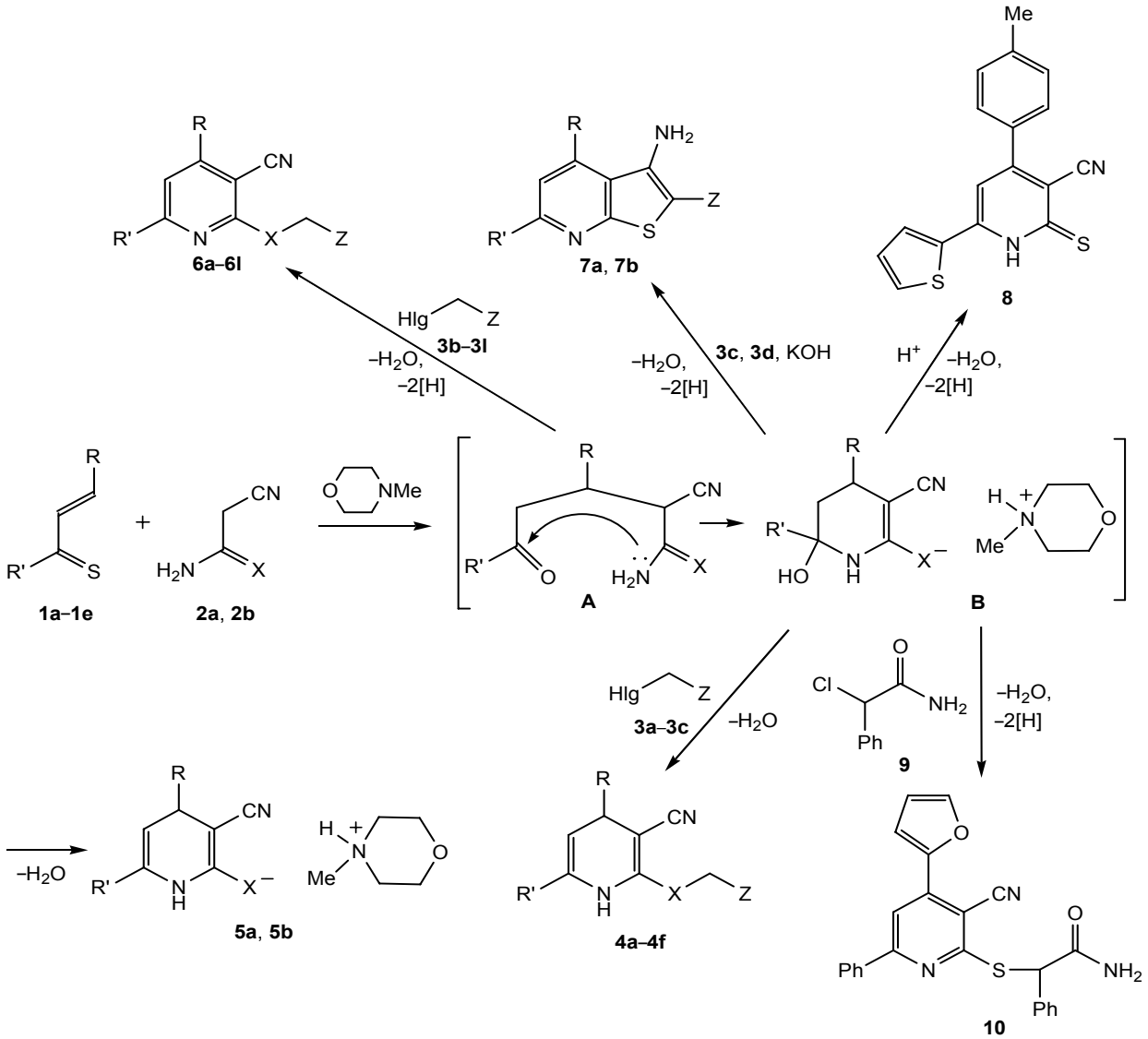
1,4-Dihydropyridine derivatives are known to exhibit a wide range of biological activity: antitumor [1, 2], antioxidant [3], and antimicrobial [4, 5]. They are used in the treatment of cardiovascular [6–9] and viral [10] diseases, and of Alzheimer disease as well [11, 12]. The main synthetic procedure for preparation of these structures is Hantzsch reaction [13–15], i.e., in the positions *3* and *5* of the dihydropyridine ring are always present electron-withdrawing substituents preventing its aromatization [16]. As examples of syntheses of 1,4-dihydropyridines lacking electron-withdrawing substituent in the position *5* may be cited reactions of chalcones with 2-cyanoethaneselenoacetamide [17] or 2-cyanoethanethioamide [18] proceeding similar to Michael additionin in the presence of amines and resulting in *N*-methylmorpholinium 4,6-diaryl-3-cyano-1,4-dihydropyridine-2-selenolates and piperidinium 4,6-diaryl-3-cyano-1,4-dihydropyridine-2-thiolates respectively.

We developed a new method for the synthesis of stable 1,4-dihydropyridines lacking electron-withdrawing substituent in the position *5*. The three-component condensation of 1,3-diaryl(heteryl)-prop-2-ene-1-ones **1a–1e** with cyanoethanethio(seleno)amides **2a** and **2b** and alkylating reagents **3a–3c** in anhydrous ethanol at 20°C in the presence of equimolar quantity of *N*-methylmorpholine afforded 2-alkylsulfanyl(selanyl)-4,6-diaryl(heteryl)-1,4-dihydropyridine-3-carbonitriles **4a–4f**. Apparently Michael adducts **A** are intermediates of this reaction undergoing the heterocyclization in salts **B**. The latter are subjected to regioselective alkylation with alkyl halides **3** at the chalcogen atom with the formation of the corresponding thio(seleno)ethers **4a–4f**. This condensation scheme is confirmed both by the isolation of salts **5a** and **5b** in the individual state and by obtaining substituted pyridines **6a–6l** and thienopyridines **7a** and **7b**, potential intermediates in designing drugs with antiviral [19] and antitumor action [20, 21].

Compounds **6** and **7** are evidently preceded by the formation of 1,4-dihydropyridines **4**, but we have failed to isolate them due the readily occurring aromatization of the dihydropyridine ring, apparently by the reaction with the air oxygen. Pyridine derivatives **6a–6l** formed as a mixture with 1,4-dihydropyridines **4**, but the recrystallization of the mixture from the glacial acetic acid afforded only compounds **6**. Substituted thieno-[2,3-*b*]pyridines **7a** and **7b** formed at the treatment of a similar mixture with a 10% water solution of KOH under conditions favoring the Thorpe–Ziegler reaction [22, 23]. Salts **5** are also unstable against oxidation. At the treatment of the reaction mixture with 10% hydrochloric acid before the stage of the addition of alkyl halide **3** 4-(4-methylphenyl)-2(1*H*)-thioxo-6-(thiophen-2-yl)pyridine-3-carbonitrile **8** was isolated.

The instability of the functionalized 2-thioxo-(selenoxo)dihydropyridine ring in acidic and basic environment is evidently a general characteristic [24–28]. The use in this condensation of an alkylating agent



1, R = R' = thiophen-2-yl (**a**); R = furan-2-yl, R' = Ph (**b**); R = thiophen-2-yl, R' = pyridin-3-yl (**c**); R = 4-methylphenyl, R' = thiophen-2-yl (**d**); R = thiophen-2-yl, R' = 4-BrC_6H_4 (**e**); **2**, X = S (**a**), Se (**b**); **3**, Hlg = I, Z = H (**a**); Hlg = Cl: Z = $CONH_2$ (**b**), 4-BrC_6H_4NHCO (**c**), CN (**d**), COOMe (**e**); Hlg = I, Z = Me (**f**); Hlg = Cl, Z = $COOCH_2Ph$ (**g**); Hlg = Br, Z = 4-MeC_6H_4CO (**h**), 2-methylphenyl (**i**), 3,4-$Cl_2C_6H_3CO$ (**j**); Hlg = Cl, Z = PhNHCO (**k**); Hlg = Br, Z = 4-BuC_6H_4CO (**l**); **4**, R = R' = thiophen-2-yl, X = S, Z = $CONH_2$ (**a**); R = furan-2-yl, R' = Ph, X = S: Z = 4-BrC_6H_4NHCO (**b**), $CONH_2$ (**c**), H (**d**); R = thiophen-2-yl, R' = 4-BrC_6H_4, X = S, Z = H (**e**); R = furan-2-yl, R' = Ph, X = Se, Z = H (**f**); **5**, R = furan-2-yl, R' = Ph, X = S (**a**); R = thiophen-2-yl, R' = pyridin-3-yl, X = Se (**b**); **6**, R = thiophen-2-yl, R' = 4-BrC_6H_4, X = S, Z = COOMe (**a**), $CONH_2$ (**b**); R = thiophen-2-yl, R' = pyridin-3-yl, X = Se, Z = CN (**c**); R = furan-2-yl, R' = Ph, X = S: Z = 4-BrC_6H_4NHCO (**d**), Me (**e**), $COOCH_2Ph$ (**f**), 4-MeC_6H_4CO (**g**), 2-MeC_6H_4 (**h**), 3,4-$Cl_2C_6H_3CO$ (**i**), COOMe (**j**), PhNHCO (**k**), 4-BuC_6H_4CO (**l**); **7**, R = furan-2-yl, R' = Ph, Z = CN (**a**); R = R' = thiophen-2-yl, Z = 4-BrC_6H_4NHCO (**b**).

2-phenyl-2-chloroacetamide **9** led to the formation of 2-phenyl-2-{[6-phenyl-4-(furan-2-yl)-3-cyanopyridin-2-yl]sulfanyl}acetamide **10**.

Spectral characteristics confirm the structure of compounds **2–8** and **10**. The IR spectra contain characteristic absorption bands of the stretching vibrations of the conjugate d cyano group in the region 2195–2224 cm^{-1}. The characteristic signals in the ^1H NMR spectra of compounds **4** are the proton signals of the 1,4-dihydropyridine ring H^4 (doublet) and N^1H (broadened singlet) in the region δ 4.52–4.71 and 9.13–10.63 ppm. The nonequivalence of the protons of the SCH_2 group (due to the lack of the free rotation of the

alkylsulfanyl substituent) resulted in splitting of the signal at 3.61–4.06 ppm in two doublets, ^2J 15.2–18.8 Hz. In the ^{1}H NMR spectra of thieno[2,3-*b*]-pyridines **7** instead of the signals of the fragment SCH_2 a signal appears from the protons of the NH_2 group as a broadened singlet in the region δ 6.28–6.54 ppm. The mass spectrum of pyridinethione **8** contains a peak of ion $[M + 2]^+$ confirming the presence of atoms S in its molecule [29].

EXPERIMENTAL

IR spectra of compounds synthesized were recorded on a FIR-spectrometer Spectrum One (Perkin Elmer) from pellets with KBr. ^{1}H and ^{13}C NMR spectra were registered on a spectrometer Bruker DRX 500 (499.95 and 125.74 MHz respectively) in DMSO-d_6, internal reference TMS. Mass spectra were obtained on spectrometers MKh-1321 (70 eV) with direct admission of the sample in the ion source (for compound **8**), and Agilent 1100 Series with a selective detector Agilent LS/MSDSL (electron impact ionization, the sample was introduced in the matrix CF_3COOH) for the other compounds. Elemental analysis was carried out on a Perkin Elmer CHN-analyzer. 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 and under UV irradiation.

Compounds (4a–4f, 6a–6l and 10). General procedure. A mixture of 10 mmol of chalcone **1a–1e**, 10 mmol of CH-acid **2a** and **2b**, and 1.1 mL (10 mmol) of *N*-methylmorpholine in 10 mL of ethanol at 20°C was stirred for 1 h, then 10 mmol of alkyl halide **3a–3l** and **9**, was added, the reaction mixture was stirred for 2 h and left standing for 24 h. Then the mixture was diluted with an equal volume of water, the separated precipitate was filtered off, washed with water, ethanol, and hexane.

2-{[4,6-Bis(thiophen-2-yl)-3-cyano-1,4-dihydropyridine-2-yl]sulfanyl}acetamide (4a). Yield 2.5 g (70%), mp 210–212°C (EtOH). IR spectrum, ν, cm^{-1}: 3365, 3298, 3202 (NH, NH_2), 2195 (C≡N), 1668 (CONH). ^{1}H NMR spectrum, δ, ppm: 3.62 d (1H, SCH_2, ^2J 17.6 Hz), 3.84 d (1H, SCH_2, ^2J 17.6 Hz), 4.71 d (1H, H^4, *J* 4.9 Hz), 5.24 d (1H, H^5, *J* 4.9 Hz), 6.94–7.48 (4H, H_{arom}), 7.66–7.92 m (3H, $2H_{arom}$, NH_2), 8.13 br.s (1H, NH_2), 10.63 br.s (1H, N^{1}H). Mass spectrum, *m/z* (I_{rel}, %): 360 (100) $[M + 1]^+$. Found, %: C 53.30; H 3.52; N 11.56. $C_{16}H_{13}N_3OS_3$. Calculated, %: C 53.46; H 3.65; N 11.69. *M* 359.491.

***N*-(4-Bromophenyl)-2-{[6-phenyl-4-(furan-2-yl)-3-cyano-1,4-dihydropyridin-2-yl]sulfanyl}-acetamide (4b)**. Yield 3.4 g (69%), mp 212–214°C (BuOH). IR spectrum, ν, cm^{-1}: 3388, 3271 (N–H), 2200 (C≡N), 1666 (CONH). ^{1}H NMR spectrum, δ, ppm: 3.99 d (1H, SCH_2, ^2J 18.8 Hz), 4.06 d (1H, SCH_2, ^2J 18.8 Hz), 4.59 d (1H, H^4, *J* 5.2 Hz), 5.15 d (1H, H^5, *J* 5.2 Hz), 6.36 d (1H, H^3_{furan}, *J* 2.9 Hz), 6.83 m (1H, H^4_{furan}), 7.14–7.76 m (7H, H_{arom}), 8.01–8.25 m (3H, H^5_{furan} and Ph), 9.67 br.s (1H, NHCO), 10.63 br.s (1H, N^{1}H). Mass spectrum, *m/z* (I_{rel}, %): 493 (100) $[M + 1]^+$. Found, %: C 58.40; H 3.54; N 8.46. $C_{24}H_{18}BrN_3O_2S$. Calculated, %: C 58.54; H 3.68; N 8.53. *M* 492.398.

2-{[6-Phenyl-4-(furan-2-yl)-3-cyano-1,4-dihydropyridin-2-yl]sulfanyl}acetamide (4c). Yield 2.4 g (70%), mp 211–213°C (BuOH). IR spectrum, ν, cm^{-1}: 3399, 3280, 3211 (NH, NH_2), 2195 (C≡N), 1660 (CONH). ^{1}H NMR spectrum, δ, ppm: 3.61 d (1H, SCH_2, ^2J 15.2 Hz), 3.88 d (1H, SCH_2, ^2J 15.2 Hz), 4.56 d (1H, H^4, *J* 5.1 Hz), 5.18 d (1H, H^5, *J* 5.1 Hz), 6.19 d (1H, H^3_{furan}, *J* 2.9 Hz), 6.40 d.d (1H, H^4_{furan}, *J* 2.4 Hz), 7.31–7.82 m (7H, Ph, NH_2), 8.28 d (3H, H^5_{furan}, *J* 1.1 Hz), 10.37 br.s (1H, N^{1}H). Mass spectrum, *m/z* (I_{rel}, %): 338 (100) $[M + 1]^+$. Found, %: C 63.95; H 4.32; N 12.29. $C_{18}H_{15}N_3O_2S$. Calculated, %: C 64.08; H 4.48; N 12.45. *M* 337.404.

2-(Methylsulfanyl)-6-phenyl-4-(furan-2-yl)-1,4-dihydropyridine-3-carbonitrile (4d). Yield 2.1 g (71%), mp 111–113°C (MeOH). IR spectrum, ν, cm^{-1}: 3300 (N–H), 2198 (C≡N). ^{1}H NMR spectrum, δ, ppm: 2.71 s (3H, SMe), 4.52 d (1H, H^4, *J* 5.0 Hz), 5.04 d (1H, H^5, *J* 5.0 Hz), 6.18 d (1H, H^3_{furan}, *J* 2.8 Hz), 6.41 d.d (1H, H^4_{furan}, *J* 2.3 Hz), 6.28–6.63 m (5H, Ph), 8.25 d (1H, H^5_{furan}, *J* 1.2 Hz), 9.37 br.s (1H, N^{1}H). Mass spectrum, *m/z* (I_{rel}, %): 295 (100) $[M + 1]^+$. Found, %: C 69.22; H 4.67; N 9.41. $C_{17}H_{14}N_2OS$. Calculated, %: C 69.36; H 4.79; N 9.52. *M* 294.378.

6-(4-Bromophenyl)-2-(methylsulfanyl)-4-(thiophen-2-yl)-1,4-dihydropyridine-3-carbonitrile (4e). Yield 2.7 g (69%), mp 136–138°C (PrOH). IR spectrum, ν, cm^{-1}: 3314 (N–H), 2202 (C≡N). ^{1}H NMR spectrum, δ, ppm: 2.72 s (3H, Me), 4.69 d (1H, H^4, *J* 5.0 Hz), 5.24 d (1H, H^5, *J* 5.0 Hz), 6.94 d (1H, $H^3_{thiophene}$, *J* 4.5 Hz), 7.25 d (2H, H_{arom}, *J* 7.5 Hz), 7.64 d (2H, H_{arom}, *J* 7.5 Hz), 8.01 d.d (1H, $H^4_{thiophene}$, *J* 6.2 Hz),

8.22 d (1H, $H^{5}_{thiophene}$, *J* 3.7 Hz), 9.21 br.s (1H, NH). Mass spectrum, *m/z* (I_{rel}, %): 390 (100) $[M + 1]^+$. Found, %: C 52.31; H 3.22; N 7.01. $C_{17}H_{13}BrN_2S_2$. Calculated, %: C 52.45; H 3.37; N 7.20. *M* 389.339.

2-(Methylselanyl)-6-phenyl-4-(furan-2-yl)-1,4-dihydropyridine-3-carbonitrile (4f). Yield 2.3 g (68%), mp 107–109°C (MeOH). IR spectrum, ν, cm^{-1}: 3314 (N–H), 2195 (C≡N). ^{1}H NMR spectrum, δ, ppm: 2.47 s (3H, Me), 4.50 d (1H, H^{4}, *J* 5.0 Hz), 5.07 d (1H, H^{5}, *J* 5.0 Hz), 6.17 d (1H, H^{3}_{furan}, *J* 2.9 Hz), 3.39 d.d (1H, H^{4}_{furan}, *J* 2.6 Hz), 7.42 br.s (5H, Ph), 7.59 d (1H, H^{5}_{furan}, *J* 1.2 Hz), 9.02 br.s (1H, NH). Mass spectrum, *m/z* (I_{rel}, %): 342 (100) $[M + 1]^+$. Found, %: C 59.71; H 4.00; N 8.02. $C_{17}H_{14}N_2OSe$. Calculated, %: C 59.83; H 4.14; N 8.21. *M* 341.274.

Methyl 2-{[6-(4-bromophenyl)-4-(thiophen-2-yl)-3-cyanopyridine-2-yl]sulfanyl}acetate (6a). Yield 3.3 g (75%), mp 169–171°C (AcOH). IR spectrum, ν, cm^{-1}: 2222 (CN), 1711 (C=O). ^{1}H NMR spectrum, δ, ppm: 3.68 s (3H, Me), 4.25 s (2H, CH_2), 7.31 d (1H, $H^{3}_{thiophene}$, *J* 4.4 Hz), 7.71 d (2H, H_{arom}, *J* 7.4 Hz), 7.81–8.23 m (5H, H_{arom}). Mass spectrum, *m/z* (I_{rel}, %): 446 (100) $[M + 1]^+$. Found, %: C 51.14; H 2.86; N 6.11. $C_{19}H_{13}BrN_2O_2S_2$. Calculated, %: C 51.24; H 2.94; N 6.29. *M* 445.360.

2-{[6-(4-Bromophenyl)-4-(thiophen-2-yl)-3-cyanopyridine-2-yl]sulfanyl}acetamide (6b). Yield 3.1 g (72%), mp 260–262°C (AcOH). IR spectrum, ν, cm^{-1}: 3386, 3221, 3195 (NH_2), 2216 (C≡N), 1669 (CONH). ^{1}H NMR spectrum, δ, ppm: 4.05 s (2H, CH_2), 7.11 d (1H, $H^{3}_{thiophene}$, *J* 4.3 Hz), 7.32 d.d (1H, $H^{4}_{thiophene}$, *J* 6.3 Hz), 7.70 d (2H, H_{arom}, *J* 7.5 Hz), 7.81–8.06 m (4H, $H^{5}_{thiophene}$, $H^{5}_{pyridine}$ and NH_2), 8.22 d (2H, H_{arom}, *J* 7.5 Hz). Mass spectrum, *m/z* (I_{rel}, %): 431 (100) $[M + 1]^+$. Found, %: C 50.16; H 2.68; N 9.60. $C_{18}H_{12}BrN_3OS_2$. Calculated, %: C 50.24; H 2.28; N 9.76. *M* 430.348.

6-[(Cyanomethyl)selanyl]-4-(thiophen-2-yl)-2,3'-bipyridine-5-carbonitrile (6c). Yield 2.6 g (68%), mp 172–174°C (AcOH). IR spectrum, ν, cm^{-1}: 2249, 2221 (C≡N). ^{1}H NMR spectrum, δ, ppm: 4.29 s (2H, CH_2), 7.35 t (1H, H_{arom}, *J* 5.3 Hz), 7.51–7.72 m (2H, H_{arom}), 7.90–8.13 m (1H, H_{arom}), 8.19 s (1H, $H^{3}_{pyridine}$), 8.56–8.82 m (2H, H_{arom}), 9.50 s (1H, $H^{1}_{pyridine}$). Mass spectrum, *m/z* (I_{rel}, %): 382 (100) $[M + 1]^+$. Found, %: C 53.42; H 2.54; N 14.51. $C_{17}H_{10}N_4SSe$. Calculated, %: C 53.55; H 2.64; N 14.69. *M* 381.321.

***N*-(4-Bromophenyl)-2-{[6-phenyl-4-(furan-2-yl)-3-cyanopyridine-2-yl]sulfanyl}acetamide (6d)**. Yield 3.7 g (75%), mp 273–275°C (AcOH). IR spectrum, ν, cm^{-1}: 3315 (N–H), 2224 (C≡N), 1678 (CONH). ^{1}H NMR spectrum, δ, ppm: 4.31 s (2H, CH_2), 6.83 d.d (1H, H^{4}_{furan}, *J* 4.4 Hz), 7.28–7.51 m (7H, H_{arom}), 7.65 d (2H, H_{arom}, *J* 7.4 Hz), 8.04 s (1H, $H^{5}_{pyridine}$), 8.17 d (2H, H_{arom}, *J* 7.4 Hz), 10.36 br.s (1H, NH). Mass spectrum, *m/z* (I_{rel}, %): 491 (100) $[M + 1]^+$. Found, %: C 58.67; H 3.14; N 8.42. $C_{24}H_{16}BrN_3O_2S$. Calculated, %: C 58.78; H 3.29; N 8.57. *M* 490.383.

6-Phenyl-4-(furan-2-yl)-2-(ethylsulfanyl)pyridine-3-carbonitrile (6e). Yield 2.5 g (81%), mp 293–295°C (AcOH). IR spectrum, ν, cm^{-1}: 2223 (C≡N). ^{1}H NMR spectrum, δ, ppm: 1.38 t (3H, Me, *J* 6.2 Hz), 3.27 q (2H, CH_2, *J* 6.2 Hz), 6.67 d (1H, H^{3}_{furan}, *J* 2.8 Hz), 7.22–7.71 m (4H, H_{arom}), 7.75–8.33 m (4H, H_{arom}). Mass spectrum, *m/z* (I_{rel}, %): 307 (100) $[M + 1]^+$. Found, %: C 70.41; H 4.55; N 9.02. $C_{18}H_{14}N_2OS$. Calculated, %: C 70.56; H 4.61; N 9.14. *M* 306.389.

Benzyl 2-{[6-phenyl-4-(furan-2-yl)-3-cyanopyridine-2-yl]sulfanyl}acetate (6f). Yield 2.8 g (65%), mp 115–117°C (AcOH). IR spectrum, ν, cm^{-1}: 2219 (C≡N), 1711 (C=O). ^{1}H NMR spectrum, δ, ppm: 4.33 s (2H, SCH_2), 5.13 s (2H, OCH_2), 6.85 d (1H, H^{3}_{furan}, *J* 2.9 Hz), 7.11–7.72 m (8H, H_{arom}), 7.95–8.33 m (5H, H_{arom}). Mass spectrum, *m/z* (I_{rel}, %): 427 (100) $[M + 1]^+$. Found, %: C 70.28; H 4.13; N 6.42. $C_{25}H_{18}N_2O_3S$. Calculated, %: C 70.41; H 4.25; N 6.57. *M* 426.497.

2-{[2-(4-Methylphenyl)-2-oxoethylsulfanyl}-6-phenyl-4-(furan-2-yl)pyridine-3-carbonitrile (6g). Yield 2.9 g (70%), mp 151–153°C (AcOH). IR spectrum, ν, cm^{-1}: 2222 (C≡N), 1703 (C=O). ^{1}H NMR spectrum, δ, ppm: 2.44 s (3H, Me), 4.97 s (2H, CH_2), 8.86 d (1H, H^{3}_{furan}, *J* 2.8 Hz), 7.19 d (2H, H_{arom}, *J* 7.9 Hz), 7.35 d (2H, H_{arom}, *J* 7.9 Hz), 7.68 d.d (1H, H^{4}_{furan}, *J* 2.4 Hz), 7.81 d (2H, H_{arom}, *J* 7.8 Hz), 7.89–8.14 m (5H, H_{arom}). Mass spectrum, *m/z* (I_{rel}, %): 411 (100) $[M + 1]^+$. Found, %: C 72.98; H 3.50; N 6.70. $C_{25}H_{18}N_2O_2S$. Calculated, %: C 73.15; H 4.42; N 6.82. *M* 410.998.

2-[(2-Methylbenzyl)sulfanyl]-6-phenyl-4-(furan-2-yl)pyridine-3-carbonitrile (6h). Yield 2.5 g (65%), mp 161–163°C (AcOH). IR spectrum, ν, cm^{-1}: 2220 (C≡N). ^{1}H NMR spectrum, δ, ppm: 2.38 s (3H, Me), 4.64 s (2H, CH_2), 6.82 d (1H, H^{3}_{furan}, *J* 2.9 Hz), 7.08–7.29 m (3H, H_{arom}), 7.31–7.52 m (6H, H_{arom}), 8.06 s (1H, $H^{5}_{pyridine}$), 8.24 m (2H, H_{arom}). Mass spectrum, *m/z* (I_{rel}, %): 383 (100) $[M + 1]^+$. Found, %: C 75.19; H 4.58; N 7.16. $C_{24}H_{18}N_2OS$. Calculated, %: C 75.37; H 4.73; N 7.32. *M* 382.487.

2{[2-(3,4-Dichlorophenyl)-2-oxoethyl]sulfanyl}-6-phenyl-4-(furan-2-yl)pyridine-3-carbonitrile (6i). Yield 3.6 g (77%), mp 129–131°C (AcOH). IR spectrum, ν, cm^{-1}: 2225 (C≡N), 1694 (C=O). ^1H NMR spectrum, δ, ppm: 4.98 s (2H, CH_2), 6.83 d (1H, H^3_{furan}, *J* 2.8 Hz), 7.12–7.58 m (5H, H_{arom}), 7.62–8.26 m (6H, H_{arom}). Mass spectrum, *m/z* (I_{rel}, %): 466 (100) $[M + 1]^+$. Found, %: C 61.84; H 2.95; N 5.91. $C_{24}H_{14}Cl_2N_2O_2S$. Calculated, %: C 61.95; H 3.03; N 6.02. *M* 465.362.

Methyl 2-{[6-phenyl-4-(furan-2-yl)-3-cyanopyridine-2-yl]sulfanyl}acetate (6j). Yield 2.8 g (80%), mp 120–122°C (AcOH). IR spectrum, ν, cm^{-1}: 2223 (C≡N), 1708 (C=O). ^1H NMR spectrum, δ, ppm: 3.66 s (3H, MeO), 4.23 s (2H, CH_2), 6.83 d (1H, H^3_{furan}, *J* 2.9 Hz), 7.32–7.76 m (4H, H_{arom}), 7.84–8.44 m (4H, H_{arom}). Mass spectrum, *m/z* (I_{rel}, %): 351 (100) $[M + 1]^+$. Found, %: C 64.98; H 3.89; N 7.88. $C_{19}H_{14}N_2O_3S$. Calculated, %: C 65.13; H 4.03; N 8.00. *M* 350.399.

***N*-Phenyl-2-{[6-phenyl-4-(furan-2-yl)-3-cyanopyridine-2-yl]sulfanyl}acetamide (6k)**. Yield 3.0 g (72%), mp 230–232°C (AcOH). IR spectrum, ν, cm^{-1}: 3330 (NH), 2226 (C≡N), 1670 (CONH). ^1H NMR spectrum, δ, ppm: 4.28 s (2H, CH_2), 6.83 d (1H, H^3_{furan}, *J* 2.8 Hz), 7.08 d (2H, H_{arom}, *J* 7.4 Hz), 7.15–7.48 m (6H, H_{arom}), 7.63 d (2H, H_{arom}, *J* 8.1 Hz), 8.08 s (1H, $H^5_{pyridine}$), 8.19 d (2H, H_{arom}, *J* 8.1 Hz), 10.44 br.s (1H, NH). Mass spectrum, *m/z* (I_{rel}, %): 415 (100) $[M + 1]^+$. Found, %: C 69.41; H 4.02; N 10.00. $C_{24}H_{17}N_3O_2S$. Calculated, %: C 69.55; H 4.13; N 10.14. *M* 414.486.

2-{[2-(4-Butylphenyl)-2-oxoethyl]sulfanyl}-6-phenyl-4-(furan-2-yl)pyridine-3-carbonitrile (6l). Yield 3.1 g (68%), mp 160–161°C (AcOH). IR spectrum, ν, cm^{-1}: 2222 (C≡N), 1711 (C=O). ^1H NMR spectrum, δ, ppm: 0.93 t (3H, Me, *J* 6.8 Hz), 1.11–1.79 m (4H, $2CH_2$), 2.71 t (2H, CH_2, *J* 5.9 Hz), 4.98 s (2H, SCH_2), 6.83 d (1H, H^3_{furan}, *J* 2.9 Hz), 7.08–7.22 m (4H, H_{arom}), 7.38 d (2H, H_{arom}, *J* 7.9 Hz), 7.66 d.d (1H, H^4_{furan}, *J* 4.8 Hz), 7.88 d (2H, H_{arom}, *J* 7.9 Hz), 7.92–8.15 m (3H, H_{arom}). Mass spectrum, *m/z* (I_{rel}, %): 453 (100) $[M + 1]^+$. Found, %: C 74.25; H 5.22; N 6.08. $C_{28}H_{24}N_2O_2S$. Calculated, %: C 74.31; H 5.35; N 6.19. *M* 452.579.

2-Phenyl-2-{[6-phenyl-4-(furan-2-yl)-3-cyanopyridin-2-yl]sulfanyl}acetamide (10). Yield 3.1 g (76%), mp 275–277°C (AcOH). IR spectrum, ν, cm^{-1}: 3395, 3311 (NH_2), 2221 (C≡N), 1669 (CONH). ^1H NMR spectrum, δ, ppm: 5.84 s (1H, SCH), 6.83 d (1H, H^3_{furan}, *J* 2.8 Hz), 7.21–7.42 m (5H, H_{arom}), 7.49–7.72 m (6H, H_{arom} and NH_2), 7.80 br.s (1H, NH_2), 8.05 s (1H, $H^5_{pyridine}$), 8.26 m (2H, H_{arom}). Mass spectrum, *m/z* (I_{rel}, %): 412 (100) $[M + 1]^+$. Found, %: C 69.95; H 4.02; N 10.09. $C_{24}H_{17}N_3O_2S$. Calculated, %: C 70.06; H 4.16; N 10.21. *M* 411.486.

***N*-Methylmorpholinium 6-phenyl-4-(furan-2-yl)-3-cyano-1,4-dihydropyridine-2-thiolate (5a)**. A mixture of 1.9 g (10 mmol) of chalcone **1b**, 1.0 g (10 mmol) of 2-cyanoethanethioamide **2a**, and 1.1 mL (10 mmol) of *N*-methylmorpholine in 20 mL of anhydrous ethanol at 20°C was stirred for 30 min and left standing for 48 h, the separated precipitate was filtered off, washed with ethanol and hexane. Yield 2.8 g (74%), red crystals, mp 217–219°C. IR spectrum, ν, cm^{-1}: 3315 (NH), 2188 (C≡N). ^1H NMR spectrum, δ, ppm: 2.58 s (3H, Me), 2.89 t (4H, CH_2NCH_2, *J* 4.4 Hz), 3.71 t (4H, CH_2OCH_2, *J* 4.4 Hz), 4.24 d (1H, $H^4_{pyridine}$, *J* 5.1 Hz), 5.19 d (1H, $H^5_{pyridine}$, *J* 5.1 Hz), 6.12 d (1H, H^3_{furan}, *J* 2.8 Hz), 6.36 d.d (1H, H^4_{furan}, *J* 2.4 Hz), 7.31–7.56 m (6H, Ph and H^5_{furan}), 9.15 br.s (1H, N^1H), the signal of the proton of the ^+NH group was not observed evidently due to the fast deuteroexchange. Found, %: C 66.01; H 5.94; N 10.88. $C_{21}H_{23}N_3O_2S$. Calculated, %: C 66.12; H 6.08; N 11.01.

***N*-Methylmorpholinium 6-(pyridine-3-yl)-4-(thiophen-2-yl)-3-cyano-1,4-dihydropyridine-2-selenolate (5b)**. A mixture of 2.2 g (10 mmol) of chalcone **1a**, 1.5 g (10 mmol) of 2-cyanoethaneselenoamide **2b**, and 1.1 mL (10 mmol) of *N*-methylmorpholine under an argon atmosphere in 20 mL of anhydrous ethanol at 20°C was stirred for 1h, the formed solution was filtered under argon through a folded filter, and the filtrate was left standing for 3 days. The precipitated yellow crystals were filtered off, washed with anhydrous ethanol and hexane. Yield 3.1 g (70%), mp 135–137°C. IR spectrum, ν, cm^{-1}: 3325 (N–H), 2186 (C≡N). ^1H NMR spectrum, δ, ppm: 2.74 s (3H, Me), 3.10 t (4H, CH_2NCH_2, *J* 4.5 Hz), 3.76 t (4H, CH_2OCH_2, *J* 4.5 Hz), 4.50 d (1H, $H^4_{dihydropyridine}$, *J* 5.0 Hz), 5.04 d (1H, $H^5_{dihydropyridine}$, *J* 5.0 Hz), 6.75–6.99 m (2H, H^3 and $H^4_{thiophene}$), 7.22–7.49 m (2H, H_{arom}), 7.53 d (1H, $H^5_{thiophene}$, *J* 3.7 Hz), 7.75–7.89 m (1H, H_{arom}), 8.64 d (1H, H_{arom}, *J* 4.8 Hz), 9.11 br.s (1H, NH), the signal of the proton of the ^+NH group was not observed evidently due to the fast deuteroexchange. Found, %: C 53.80; H 4.85; N 12.42. $C_{20}H_{22}OSSe$. Calculated, %: C 53.93; H 4.98; N 12.58.

3-Amino-4-(thiophen-2-yl)-6-phenylthieno[2,3-*b*]-pyridine-2-carbonitrile (7a). A mixture of 1.9 g (10 mmol) of chalcone **1b**, 1.0 g (10 mmol) of 2-

cyanoethanethioamide **2a**, and 1.1 mL (10 mmol) of *N*-methylmorpholine in 30 mL of ethanol at 20°C was stirred for 1 h, 10 mmol of α-chloroacetonitrile **3d** was added, the mixture was stirred for 1 h and left standing for 24 h. Then at stirring 15 mL of DMF and 5.6 mL (10 mmol) of 10% aqueous KOH solution was added to the reaction mixture, it was stirred for 4 h and diluted with an equal volume of water. The formed precipitate was filtered off, washed with water, ethanol, and hexane. Yield 2.4 g (77%), yellow powder, mp 192–194°C (BuOH). IR spectrum, ν, cm^{-1}: 3385, 3311, 3205 (NH_2), 2209 (C≡N), 1642 [δ(NH_2)]. ^1H NMR spectrum, δ, ppm: 6.54 br.s (2H, NH_2), 6.85 d (1H, H^3_{furan}, *J* 3.0 Hz), 7.32 d.d (1H, $H^4_{thiophene}$, *J* 6.0 Hz), 7.42–7.64 m (4H, H_{arom}), 8.13 s (1H, $H^5_{pyridine}$), 8.15–8.30 m (2H, H_{arom}). Mass spectrum, *m/z* (I_{rel}, %): 318 (100) $[M + 1]^+$. Found, %: C 67.96; H 3.32; N 13.14. $C_{18}H_{11}N_3OS$. Calculated, %: C 68.12; H 3.49; N 13.24. *M* 317.342.

***N*-(4-Bromophenyl)-3-amino-4,6-di(thiophen-2-yl)-thieno[2,3-*b*]pyridine-2-carboxcamide (7b)** was obtained similarly from 2.2 g (10 mmol) of chalcone **1a** and 2.5 g (10 mmol) of *N*-(4-bromophenyl)-α-chloroacetamide **3c**. Yield 3.6 g (71%), yellow powder, mp 243–245°C (BuOH). IR spectrum, ν, cm^{-1}: 3398, 3300, 3214 (NH, NH_2), 1668 (CONH), 1644 [δ(NH_2)]. ^1H NMR spectrum, δ, ppm: 6.28 br.s (2H, NH_2), 7.11 t (1H, $H^4_{thiophene}$, *J* 5.1 Hz), 7.23 t (1H, $H^{4'}_{thiophene}$, *J* 5.0 Hz), 7.03 d (1H, $H^3_{thiophene}$, *J* 4.5 Hz), 7.35 d (2H, Ar, *J* 7.5 Hz), 7.48 d (1H, $H^{3'}_{thiophene}$, *J* 4.5 Hz), 7.58 s (1H, $H^5_{pyridine}$), 7.61 d (1H, $H^5_{thiophene}$, *J* 3.5 Hz), 7.69 d (2H, Ar, *J* 7.5 Hz), 7.76 d (1H, $H^{5'}_{thiophene}$, *J* 3.5 Hz), 9.15 br.s (1H, NH). Mass spectrum, *m/z* (I_{rel}, %): 514 (92) $[M + 2]^+$, 512 (100) $[M]^+$. Found, %: C 51.42; H 2.60; N 8.04. $C_{22}H_{14}BrN_3OS_3$. Calculated, %: C 51.56; H 2.75; N 8.20. *M* 512.472.

4-(2-Methylphenyl)-2-thioxo-6-(thiophen-2-yl)-1,2-dihydropyridine-3-carbonitrile (8). A mixture of 2.3 g (10 mmol) of chalcone **1d**, 1.0 g (10 mmol) of 2-cyanoethanethioamide **2a**, and 1.1 mg (10 mmol) of *N*-methylmorpholine in 20 mL of ethanol at 20°C was stirred for 1 h and left standing for 24 h. Then the reaction mixture was diluted with 10% hydrochloric acid till pH 5, and the mixture was left standing for 48 h. The separated precipitate was filtered off, washed with water, ethanol, and hexane. Yield 2.4 g (77%), yellow powder, mp 236–238°C (AcOH). IR spectrum, ν, cm^{-1}: 3345 (NH), 2220 (C≡N). ^1H NMR spectrum, δ, ppm: 2.41 s (3H, Me), 6.99 s (1H, $H^5_{pyridine}$), 7.24 t (1H, $H^4_{thiophene}$, *J* 5.2 Hz), 7.35 d (2H, Ar, *J* 7.7 Hz), 7.61 d (2H, Ar, *J* 7.7 Hz), 7.95 d (1H, $H^3_{thiophene}$, *J* 4.5 Hz), 8.18 d (1H, $H^5_{thiophene}$, *J* 3.6 Hz), 13.9 br.s (1H, NH). Mass spectrum, *m/z* (I_{rel}, %): 310 (11) $[M + 2]^+$, 309 (16) $[M + 1]^+$, 308 (100) $[M]^+$, 307 (25) $[M - 1]^+$, 293 (26) $[M - Me]^+$, 275 (9), 264 (7), 233 (5), 134 (8), 140 (7), 113 (91), 100 (7), 91 (5) $[C_6H_4Me]^+$, 89 (7), 60 (8). Found, %: C 66.04; H 3.81; N 8.95. $C_{17}H_{12}N_2S_2$. Calculated, %: C 66.20; H 3.92; N 9.08. *M* 308.427.

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