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Dedicated to Full Member of the Russian Academy of Sciences V.A. Tartakovskii on the 75th anniversary of his birth

Synthesis of Fused Heterocyclic Compounds on the Basis of 2-Thioxo-1,3-thiazolidin-4-ones

V. N. Yarovenko[a], A. S. Nikitina[b], I. V. Zavarzin[a], M. M. Krayushkin[a], and L. V. Kovalenko[b]

[a] *Zelinskii Institute of Organic Chemistry, Russian Academy of Sciences, Leninskii pr. 47, Moscow, 119991 Russia*
e-mail: yarov@ioc.ac.ru

[b] *Mendeleev Russian University of Chemical Technology, Moscow, Russia*

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Abstract—Methods for the preparation of various fused heterocyclic systems having thiazolothiadiazole, furothiazole, pyrazolothiazole, thiazolopyridine, pyranothiazole, and chromenopyranothiazole skeletons were developed using 2-thioxo-1,3-thiazolidin-4-ones as initial compounds.

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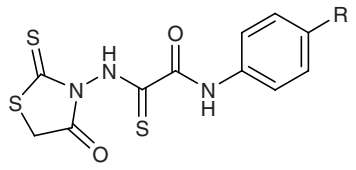
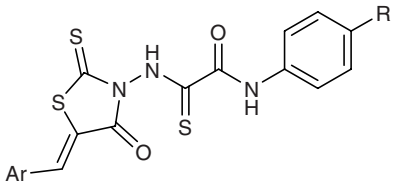
We recently synthesized for the first time 2-thioxo-1,3-thiazolidin-4-ones **I** by reaction of 2-hydrazino-2-thioxoacetamides with trithiocarbonyl diglycolic acid [1] and obtained their 5-arylmethylidene derivatives **II** [2] which can be readily converted into various heterocycles. In the present work we examined the reactivity of compounds **I** and **II**.



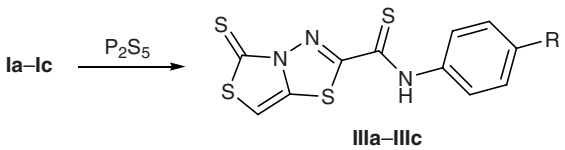
I



II

By heating thiazolidines **Ia**–**Ic** with Lawesson's reagent or diphosphorus pentasulfide in toluene we obtained 75–85% of thiazolo[4,3-*b*][1,3,4]thiadiazole-5-thiones **IIIa**–**IIIc** (Scheme 1). The reactions of compounds **Ia**–**Ic** with chloroacetic acid in methanol in the presence of sodium methoxide involved the methylene and carbonyl groups in the former and led to the formation of 60–65% of 2-thioxo-2,3,5,6-tetrahydrofuro[2,3-*d*][1,3]thiazol-6-ones **IVa**–**IVc** (Scheme 2). 5-Benzylidene rhodanine derivatives **IIa**–**IIc** (Ar = Ph) having a conjugated carbonyl group reacted with such difunctional nucleophile as phenylhydrazine in the presence of sodium acetate to give tetrahydro-5*H*-pyrazolo[3,4-*d*][1,3]thiazole-5-thiones **Va**–**Vc** in 55–65% yield. The reactions in anhydrous ethanol were complete in 3.5 h, whereas in boiling acetic acid 7 h was necessary to attain the same yields (Scheme 3). 5-Oxo-2-thioxo-2,3,4,5,6,7-hexahydro[1,3]thiazolo[4,5-*b*]-

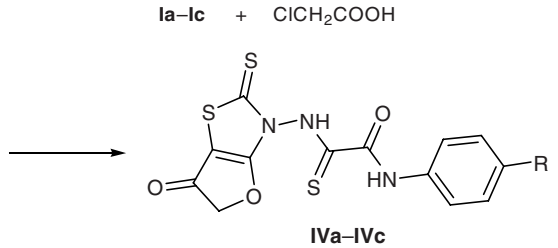
Scheme 1.



IIIa–IIIc

R = H (**a**), Cl (**b**), MeO (**c**).

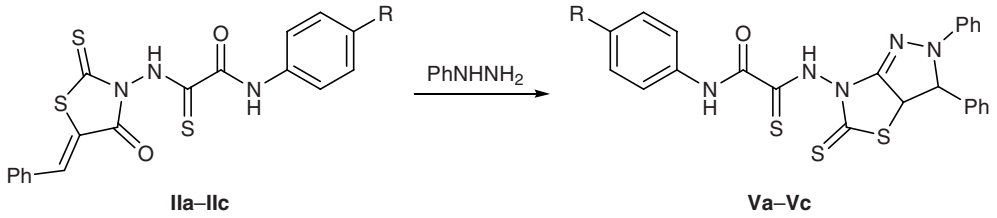
Scheme 2.



IVa–IVc

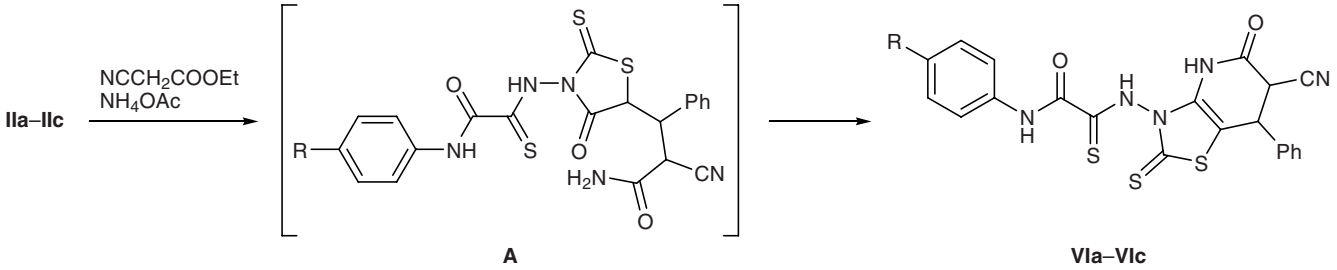
R = H (**a**), Cl (**b**), MeO (**c**).

Scheme 3.



R = H (**a**), Cl (**b**), MeO (**c**).

Scheme 4.

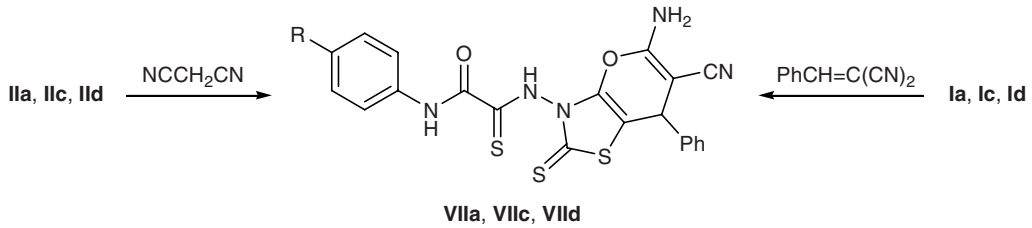


R = H (**a**), Cl (**b**), MeO (**c**).

pyridine-6-carbonitriles **VIa**–**VIc** were obtained in 50–55% yield by heating compounds **IIa**–**IIc** with ethyl cyanoacetate in boiling acetic acid in the presence of ammonium acetate (reaction time 4 h; Scheme 4). Presumably, the first stage of the process is base-catalyzed condensation of ethyl cyanoacetate at the α,β-unsaturated ketone fragment of **II**, and the subsequent intramolecular cyclization of Michael adduct **A** with elimination of water leads to the final product. The yield of fused heterocycles **VIa**–**VIc** can be increased to a considerable extent by carrying out the reaction under microwave (MW) irradiation. The optimal power of MW irradiation was found to be 210 W. Higher power induced tarring of the reaction mixture, while at lower power the reaction time was considerably longer. The optimal solvent for the MW-activated synthesis was acetic acid. By reactions of benzylidene derivatives **IIa**–**IIc** with ethyl cyanoacetate and ammonium acetate in acetic acid under MW irradiation (210 W; reaction time 45 min) we obtained substituted 5-oxo-2-thioxo-2,3,4,5,6,7-hexahydro[1,3]thiazolo[4,5-*b*]pyridine-6-carbonitriles **VIa**–**VIc** in 88–90% yield.

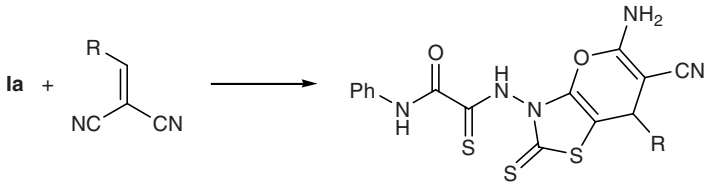
Compounds **IIa**–**IIc** failed to react with maleic anhydride and malononitrile under the conditions reported in [3]. The reaction occurred neither at room temperature nor on heating in acetic acid, and only the initial compounds were isolated from the reaction mixtures. We succeeded in synthesizing 5-amino-2-thioxo-3,7-dihydro-2*H*-pyrano[2,3-*d*][1,3]thiazole-6-carbonitriles **VIIa**, **VIIc**, and **VIId** in fairly moderate yields (25–35%) when compounds **IIa**, **IIc**, and **IId** were heated with malononitrile in DMF in the presence of triethylamine for 10 h or in anhydrous ethanol for 3 h (yield 30–35%; Scheme 5). The optimal conditions for the same reaction activated by microwave irradiation were as follows: MW power 210 W, reaction time 45 min; in this case, the yields of pyranothiazoles **VIIa**, **VIIc**, and **VIId** were 85–87%. Alternatively,

Scheme 5.



R = H (**a**), MeO (**c**), O_2N (**d**).

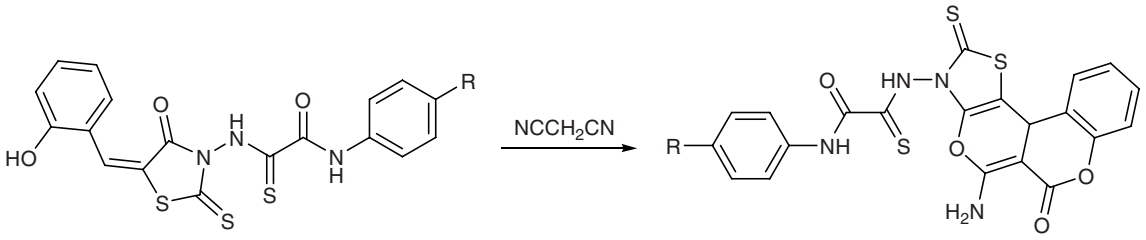
Scheme 6.



VIIe, **VIIf**

R = 2-thienyl (**e**), 5-nitrofuran-2-yl (**f**).

Scheme 7.



IIe–IIg **VIIIa–VIIIc**

R = H (**a**, **e**), Cl (**b**, **f**), MeO (**c**, **g**).

compounds **VII** can be synthesized by heating a mixture of benzylidenemalononitrile and compound **Ia**, **Ic**, or **Id** in boiling ethanol in the presence of piperidine. Under these conditions, the yields were 50–55%.

Application of the above approach simplifies the synthesis of various 2*H*-pyrano[2,3-*d*][1,3]thiazoles **VII** and increases their yield calculated on the initial rhodanine. For example, 5-nitro-2-furyl- and 2-thienyl-substituted 2*H*-pyrano[2,3-*d*][1,3]thiazole derivatives **VIIe** and **VIIf** were thus prepared in 55–60% yield (Scheme 6).

The presence of a reactive substituent in the *ortho* position of the benzene ring in the arylmethylidene fragment of molecule **II** provides the possibility for subsequent heterocyclization. 2-Hydroxybenzylidene derivatives **IIe**–**IIg** (Ar = 2-HOC_6H_4) reacted with malononitrile to give fused chromeno[4′,3′:4,5]pyrano-[2,3-*d*]thiazol-6-ones **VIIIa**–**VIIIc** in 33–35% yield (Scheme 7). Presumably, instability of arylmethylidene-substituted rhodanines in basic medium at elevated temperature is responsible for the low yields of the cyclocondensation products. By carrying out the process under MW irradiation (210 W, 1.5 h) we succeeded in raising the yields of **VIIIa**–**VIIIc** to 80–85%.

The structure of the isolated compounds was confirmed by the ^{1}H and ^{13}C NMR and mass spectra.

Thus we have developed convenient synthetic approaches to various fused heterocyclic compounds on the basis of substituted rhodanine derivatives. A strong positive effect of microwave irradiation on the reactions of 5-arylmethylidene-substituted rhodanines with malononitrile derivatives has been demonstrated for the first time.

EXPERIMENTAL

The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AC-300 spectrometer (300 MHz for ^{1}H) using DMSO-d_6 as solvent. The mass spectra (electron impact, 70 eV) were obtained on a Kratos MS-30 instrument with direct sample admission into the ion source (accelerating voltage 1.75 kV). The melting points were determined on a Boetius hot stage and were not corrected. The reaction mixtures were analyzed, and the purity of products was checked, by TLC on Merck 60 F_{254} plates (eluent ethyl acetate–hexane, 1:1 by volume). Microwave-assisted reactions were carried out in a Rolsen MS1770SA domestic oven.

***N*-Phenyl-5-thioxo[1,3]thiazolo[4,3-*b*][1,3,4]thiadiazole-2-carbothioamide (IIIa).** A mixture of 0.3 g (1 mmol) of rhodanine **Ia** and 0.33 g (1.5 mmol) of phosphorus(V) sulfide in 25 ml of dioxane was heated for 4 h under reflux. The mixture was cooled and pured into water, and the precipitate was filtered off and recrystallized from ethanol–petroleum ether (4:1 by volume). Yield 0.26 g (85%), dark red crystals, mp 187–188°C. ^{1}H NMR spectrum, δ, ppm: 7.05 s

(1H, 7-H), 7.2 t (1H, H_{arom}, J = 7.6 Hz), 7.45 t (2H, H_{arom}, J = 7.6 Hz), 7.9 d (2H, H_{arom}, J = 7.6 Hz), 10.6 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 102.44 (C^7), 122.21 (C^o), 128.25 (C^m), 129.39 (C^p), 140.52 (C^i), 157.16 and 163.36 (C^2, C^{7a}), 172.96 and 185.40 (C=S). Mass spectrum: m/z 309 (I_{rel} 89%) $[M]^+$. Found, %: C 42.76; H 2.24; N 13.55; S 41.48. $C_{11}H_7N_3S_4$. Calculated, %: C 42.70; H 2.28; N 13.58; S 41.45.

Compounds **IIIb** and **IIIc** were synthesized in a similar way.

***N*-(4-Chlorophenyl)-5-thioxo[1,3]thiazolo[4,3-*b*]-[1,3,4]thiadiazole-2-carbothioamide (IIIb).** Yield 77%, dark red crystals, mp 153–154°C. ^1H NMR spectrum, δ, ppm: 7.05 s (1H, 7-H), 7.5 d (2H, H_{arom}, J = 8.7 Hz), 7.9 d (2H, H_{arom}, J = 8.7 Hz), 10.45 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 101.38 (C^7), 123.83 (C^o), 129.04 (C^m), 133.72 (C^p), 140.47 (C^i), 157.21 and 163.44 (C^2, C^{7a}), 173.38 and 184.532 (C=S). Mass spectrum: m/z 343 (I_{rel} 76%) $[M]^+$. Found, %: C 38.46; H 1.80; Cl 10.29; N 12.19; S 37.33. $C_{11}H_6ClN_3S_4$. Calculated, %: C 38.42; H 1.76; Cl 10.31; N 12.22; S 37.29.

***N*-(4-Methoxyphenyl)-5-thioxo[1,3]thiazolo-[4,3-*b*][1,3,4]thiadiazole-2-carbothioamide (IIIc).** Yield 83%, dark red crystals, mp 179–180°C. ^1H NMR spectrum, δ, ppm: 3.75 s (3H, OCH_3), 6.9 d (2H, H_{arom}, J = 8.9 Hz), 7.15 s (1H, 7-H), 7.7 d (2H, H_{arom}, J = 9.0 Hz), 9.9 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 55.47 (OCH_3), 101.57 (C^7), 114.03 (C^m), 124.40 (C^o), 135.63 (C^i), 157.16 and 163.40 (C^2, C^{7a}), 160.77 (C^p), 172.20 and 184.40 (C=S). Mass spectrum: m/z 339 (I_{rel} 81%) $[M]^+$. Found, %: C 42.44; H 2.62; N 12.33; S 37.84. $C_{12}H_9N_3OS_4$. Calculated, %: C 42.46; H 2.67; N 12.38; S 37.78.

2-(6-Oxo-2-thioxo-2,3,5,6-tetrahydrofuro[2,3-*d*]-[1,3]thiazol-3-ylamino)-*N*-phenyl-2-thioxoacetamide (IVa). A mixture of 0.1 g (0.34 mmol) of compound **Ia**, 0.038 g (0.408 mmol) of chloroacetic acid, and 0.02 g (0.374 mmol) of sodium methoxide in 10 ml of methanol was heated for 6 h under reflux. The mixture was cooled, poured into water, and acidified to pH 5 by adding hydrochloric acid. The precipitate was filtered off and recrystallized from aqueous ethanol. Yield 0.071 g (60%), light yellow crystals, mp 115–116°C. ^1H NMR spectrum, δ, ppm: 4.7 s (2H, CH_2), 7.2 t (1H, H_{arom}, J = 7.6 Hz), 7.45 t (2H, H_{arom}, J = 7.6 Hz), 7.9 d (2H, H_{arom}, J = 7.6 Hz), 9.8 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 78.67 (CH_2), 103.16 and 156.60 (C^{3a}, C^{6a}), 121.18 (C^o), 125.88 (C^p), 132.26 (C^m), 141.19 (C^i), 167.77 and 178.663 (C=O), 180.74 and 189.94 (C=S). Mass spectrum: m/z 351 (I_{rel} 97%) $[M]^+$. Found, %: C 44.46; H 2.54; N 11.93; S 27.41. $C_{13}H_9N_3O_3S_3$. Calculated, %: C 44.43; H 2.58; N 11.96; S 27.37.

Compounds **IVb** and **IVc** were synthesized in a similar way.

***N*-(4-Chlorophenyl)-2-(6-oxo-2-thioxo-2,3,5,6-tetrahydrofuro[2,3-*d*][1,3]thiazol-3-ylamino)-2-thioxoacetamide (IVb).** Yield 58%, light yellow crystals, mp 132–133°C. ^1H NMR spectrum, δ, ppm: 4.55 s (2H, CH_2), 7.4 d (2H, H_{arom}, J = 8.7 Hz), 7.7 d (2H, H_{arom}, J = 8.7 Hz), 9.9 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 78.77 (CH_2), 103.15 and 156.61 (C^{3a}, C^{6a}), 121.23 (C^o), 129.61 (C^m), 130.68 (C^p), 138.98 (C^i), 167.43 and 178.58 (C=O), 181.36 and 190.00 (C=S). Mass spectrum: m/z 385 (I_{rel} 85%) $[M]^+$. Found, %: C 40.52; H 2.03; Cl 9.15; N 10.85; S 24.96. $C_{13}H_8ClN_3O_3S_3$. Calculated, %: C 40.47; H 2.09; Cl 9.19; N 10.89; S 24.93.

***N*-(4-Methoxyphenyl)-2-(6-oxo-2-thioxo-2,3,5,6-tetrahydrofuro[2,3-*d*][1,3]thiazol-3-ylamino)-2-thioxoacetamide (IVc).** Yield 55%, light yellow crystals, mp 96–97°C. ^1H NMR spectrum, δ, ppm: 3.7 s (3H, OCH_3), 4.6 s (2H, CH_2), 6.9 d (2H, H_{arom}, J = 8.92 Hz), 7.7 d (2H, H_{arom}, J = 9.0 Hz), 9.9 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 55.40 (OCH_3), 78.76 (CH_2), 103.154 and 156.99 (C^{3a}, C^{6a}), 116.71 (C^m), 121.25 (C^o), 135.66 (C^i), 155.12 (C^p), 167.56 and 178.63 (C=O), 180.48 and 190.11 (C=S). Mass spectrum: m/z 381 (I_{rel} 91%) $[M]^+$. Found, %: C 44.14; H 2.87; N 10.97; S 25.24. $C_{14}H_{11}N_3O_4S_3$. Calculated, %: C 44.08; H 2.91; N 11.02; S 25.22.

2-(2,3-Diphenyl-5-thioxo-3,3a,5,6-tetrahydro-2*H*-pyrazolo[3,4-*d*][1,3]thiazol-6-ylamino)-*N*-phenyl-2-thioxoacetamide (Va). A mixture of 0.05 g (0.13 mmol) of benzylidenethiazolidine **IIa**, 0.025 g (0.31 mmol) of sodium acetate, and 0.014 g (0.13 mmol) of phenylhydrazine in 7 ml of anhydrous ethanol was heated for 3.5 h under reflux (on a water bath). The mixture was cooled, and the precipitate was filtered off, washed with ethanol, and recrystallized from acetic acid. Yield 0.063 g (57%), dark red crystals, mp 226–227°C. ^1H NMR spectrum, δ, ppm: 4.65 d (1H, CH, J = 6.75 Hz), 5.7 d (1H, CH, J = 9.0 Hz), 6.8–7.7 m (15H, H_{arom}), 9.9 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 51.82 and 69.96 (C^3, C^{3a}), 114.20, 121.74, 128.35, 119.45, 125.68, 126.59, 129.22, 129.75, 132.22 (C_{arom}), 138.09, 141.20, 147.40 (C_{arom}), 145.60 (C^{6a}), 167.77 (C=O), 184.55 and 194.95 (C=S). Mass spectrum, m/z (I_{rel}, %): 310 (45),

178 (33). Found, %: C 58.92; H 3.87; N 14.35; S 19.62. $C_{24}H_{19}N_5OS_3$. Calculated, %: C 58.87; H 3.91; N 14.30; S 19.65.

Compounds **Vb** and **Vc** were synthesized in a similar way.

***N*-(4-Chlorophenyl)-2-(2,3-diphenyl-5-thioxo-3,3a,5,6-tetrahydro-2*H*-pyrazolo[3,4-*d*][1,3]thiazol-6-ylamino)-2-thioxoacetamide (Vb).** Yield 62%, dark red crystals, mp 184–185°C. ^{1}H NMR spectrum, δ, ppm: 4.6 d (1H, CH, J = 6.75 Hz), 5.7 d (1H, CH, J = 9.0 Hz), 6.8–7.7 m (14H, H_{arom}), 9.7 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 51.81 and 69.95 (C^3, C^{3a}), 114.20, 121.22, 128.47, 119.44, 126.65, 129.43, 129.56, 129.68 (C_{arom}), 130.64 (C_{arom}), 138.09, 138.84, 147.36 (C_{arom}), 145.59 (C^{6a}), 167.69 (C=O), 184.67 and 194.97 (C=S). Mass spectrum, *m/z* (I_{rel}, %): 310 (39), 214 (42). Found, %: C 55.06; H 3.42; Cl 6.73; N 13.42; S 18.34. $C_{24}H_{18}ClN_5OS_3$. Calculated, %: C 55.00; H 3.46; Cl 6.76; N 13.36; S 18.35.

2-(2,3-Diphenyl-5-thioxo-3,3a,5,6-tetrahydro-2*H*-pyrazolo[3,4-*d*][1,3]thiazol-6-ylamino)-*N*-(4-methoxyphenyl)-2-thioxoacetamide (Vc). Yield 55%, dark red crystals, mp 213–214°C. ^{1}H NMR spectrum, δ, ppm: 3.7 s (3H, OCH_3), 4.6 d (1H, CH, J = 6.72 Hz), 5.75 d (1H, CH, J = 8.95 Hz), 6.9–7.7 m (14H, H_{arom}), 9.7 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 51.82 and 69.96 (C^3, C^{3a}), 55.43 (OCH_3), 114.21, 121.25, 128.48, 116.72, 129.50, 129.67, 119.45, 126.67 (C_{arom}), 135.63, 138.10, 147.40 (C_{arom}), 145.60 (C^{6a}), 167.78 (C=O), 184.71 and 194.98 (C=S). Mass spectrum, *m/z* (I_{rel}, %): 310 (41), 210 (55). Found, %: C 57.83; H 4.02; N 13.54; S 18.48. $C_{25}H_{21}N_5O_2S_3$. Calculated, %: C 57.78; H 4.07; N 13.48; S 18.51.

2-(6-Cyano-5-oxo-7-phenyl-2-thioxo-2,3,4,5,6,7-hexahydro[1,3]thiazolo[4,5-*b*]pyridin-3-ylamino)-*N*-phenyl-2-thioxoacetamide (VIa). *a*. A mixture of 0.021 g (0.19 mmol) of ethyl cyanoacetate, 0.075 g (0.19 mmol) of benzylidenerhodanine **IIa**, and 0.12 g (1.52 mmol) of ammonium acetate in 10 ml of acetic acid was heated for 4 h under reflux. The product was purified by column chromatography using EtOAc–petroleum ether (1:3) as eluent. Yield 0.047 g (53%).

b. An ampule was charged with a mixture of 0.021 g (0.19 mmol) of ethyl cyanoacetate, 0.075 g (0.19 mmol) of compound **IIa**, and 0.12 g (1.52 mmol) of ammonium acetate in 1.5 ml of acetic acid. The ampule was placed in a microwave oven and irradiated for 45 min at a power of 210 W. The mixture was cooled and poured into water, and the precipitate was filtered off and recrystallized from aqueous ethanol. Yield 0.078 g (89%), dark yellow crystals, mp 134–135°C. ^{1}H NMR spectrum, δ, ppm: 7.1–7.6 m (10H, H_{arom}), 10.3 s (1H, NH), 12.4 s (1H, N^4H). ^{13}C NMR spectrum, δ_C, ppm: 95.67, 101.53, 137.17, 148.38, 115.52 (CN), 121.73, 125.88, 127.12, 129.54, 131.00, 132.34, 138.96, 141.24 (C_{arom}), 161.22 and 165.29 (C=O), 169.97 and 194.64 (C=S). Mass spectrum, *m/z* (I_{rel}, %): 286 (57), 179 (40). Found, %: C 54.36; H 2.61; N 12.13; S 20.67. $C_{21}H_{12}N_4O_3S_3$. Calculated, %: C 54.30; H 2.60; N 12.06; S 20.71.

Compounds **VIb** and **VIc** were synthesized in a similar way.

***N*-(4-Chlorophenyl)-2-(6-cyano-5-oxo-7-phenyl-2-thioxo-2,3,4,5,6,7-hexahydro[1,3]thiazolo[4,5-*b*]-pyridin-3-ylamino)-2-thioxoacetamide (VIb).** Yield 90% (*b*), dark yellow crystals, mp 169–170°C. ^{1}H NMR spectrum, δ, ppm: 7.1–7.7 m (9H, H_{arom}), 10.25 s (1H, NH), 12.3 s (1H, N^4H). ^{13}C NMR spectrum, δ_C, ppm: 95.67, 101.55, 137.15, 148.37, 115.50 (CN), 121.26, 127.11, 129.39, 129.74, 131.06, 130.64, 138.85, 138.99 (C_{arom}), 161.20 and 165.31 (C=O), 169.86 and 194.63 (C=S). Mass spectrum, *m/z* (I_{rel}, %): 286 (49), 214 (45). Found, %: C 50.61; H 2.25; Cl 7.07; N 11.28; S 19.23. $C_{21}H_{11}ClN_4O_3S_3$. Calculated, %: C 50.55; H 2.22; Cl 7.10; N 11.23; S 19.28.

2-(6-Cyano-5-oxo-7-phenyl-2-thioxo-2,3,4,5,6,7-hexahydro[1,3]thiazolo[4,5-*b*]pyridin-3-ylamino)-*N*-(4-methoxyphenyl)-2-thioxoacetamide (VIc). Yield 90% (*b*), dark yellow crystals, mp 147–148°C. ^{1}H NMR spectrum, δ, ppm: 3.7 s (3H, OCH_3), 6.9–7.7 m (9H, H_{arom}), 10.1 s (1H, NH), 12.2 s (1H, N^4H). ^{13}C NMR spectrum, δ_C, ppm: 54.42 (OCH_3), 95.85, 101.64, 137.16, 148.35, 115.49 (CN), 116.71, 121.26, 127.12, 129.52, 130.93, 135.64, 138.94, 156.11 (C_{arom}), 161.18 and 165.29 (C=O), 169.98 and 194.65 (C=S). Mass spectrum, *m/z* (I_{rel}, %): 287 (63), 210 (77). Found, %: C 53.49; H 2.86; N 11.37; S 19.41. $C_{22}H_{14}N_4O_4S_3$. Calculated, %: C 53.43; H 2.85; N 11.33; S 19.45.

2-(5-Amino-6-cyano-7-phenyl-2-thioxo-3,7-dihydro-2*H*-pyrano[2,3-*d*][1,3]thiazol-3-ylamino)-*N*-phenyl-2-thioxoacetamide (VIIa). *a*. A mixture of 0.075 g (0.19 mmol) of compound **IIa** and 0.013 g (0.19 mmol) of malononitrile in 10 ml of anhydrous ethanol containing a few drops of triethylamine was heated for 3 h under reflux. The product was purified by column chromatography using ethyl acetate–petroleum ether (1:3) as eluent. Yield 0.023 g (26%).

b. A mixture of 0.1 g (0.65 mmol) of 2-benzylidenemalononitrile, 0.19 g (0.65 mmol) of compound **Ia**, and several drops of piperidine in 10 ml of anhy-

drous ethanol was heated for 45 under reflux (water bath). The mixture was cooled to room temperature, poured into water, and neutralized to pH 6 with hydrochloric acid, and the precipitate was filtered off and recrystallized from aqueous ethanol. Yield 0.16 g (53%).

c. An ampule was charged with a mixture of 0.075 g (0.19 mmol) of compound **IIa** and 0.013 g (0.19 mmol) of malononitrile in 1.5 ml of acetic acid. The ampule was placed in a microwave oven and was irradiated for 45 min at a power of 210 W. The mixture was cooled and poured into water, and the precipitate was filtered off and recrystallized from aqueous ethanol. Yield 0.075 g (85%), yellow crystals, mp 145–146°C. ^{1}H NMR spectrum, δ, ppm: 4.5 s (1H, 7-H), 7.1–7.8 m (10H, H_{arom}), 9.85 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 33.97 (C^7); 55.14, 95.51, 143.55, 158.81 (C^{3a}, C^5, C^6, C^{7a}); 121.73, 125.89, 129.25, 130.25, 132.26, 141.20, 145.88 (C_{arom}); 160.13 (C=O); 169.78, 187.29 (C=S). Mass spectrum, *m*/*z* (I_{rel}, %): 287 (35), 179 (47). Found, %: C 54.23; H 3.27; N 15.08; S 20.63. $C_{21}H_{15}N_5O_2S_3$. Calculated, %: C 54.18; H 3.25; N 15.04; S 20.66.

Compounds **VIIc**–**VIIf** were synthesized in a similar way.

2-(5-Amino-6-cyano-7-phenyl-2-thioxo-3,7-dihydro-2*H*-pyrano[2,3-*d*][1,3]thiazol-3-ylamino)-*N*-(4-methoxyphenyl)-2-thioxoacetamide (VIIc). Yield 82% (*c*), yellow crystals, mp 155–156°C. ^{1}H NMR spectrum, δ, ppm: 3.7 s (3H, OCH_3), 4.55 s (1H, 7-H), 6.9–7.6 m (9H, H_{arom}), 9.7 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 33.95 (C^7); 55.14, 95.51, 143.55, 158.82 (C^{3a}, C^5, C^6, C^{7a}); 55.45 (OCH_3); 116.70, 121.26, 125.72, 129.24, 130.27, 153.63, 145.89, 155.99 (C_{arom}); 160.25 (C=O); 169.77, 187.26 (C=S). Mass spectrum, *m*/*z* (I_{rel}, %): 287 (33), 210 (40). Found, %: C 53.37; H 3.47; N 14.16; S 19.39. $C_{22}H_{17}N_5O_3S_3$. Calculated, %: C 53.32; H 3.46; N 14.13; S 19.41.

2-(5-Amino-6-cyano-7-phenyl-2-thioxo-3,7-dihydro-2*H*-pyrano[2,3-*d*][1,3]thiazol-3-ylamino)-*N*-(4-nitrophenyl)-2-thioxoacetamide (VIId). Yield 80% (*c*), yellow crystals, mp 178–179°C. ^{1}H NMR spectrum, δ, ppm: 4.5 s (1H, 7-H), 7.1–8.2 m (9H, H_{arom}), 9.4 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 33.95 (C^7); 55.15, 95.50, 143.61, 158.91 (C^{3a}, C^5, C^6, C^{7a}); 118.75 (CN); 119.64, 125.52, 125.86, 129.24, 130.26, 143.50, 145.80, 146.01 (C_{arom}); 160.29 (C=O); 169.77, 187.34 (C=S). Mass spectrum, *m*/*z* (I_{rel}, %): 287 (35), 224 (56). Found, %: C 49.45; H 2.78; N 16.50; S 18.80. $C_{21}H_{14}N_6O_4S_3$. Calculated, %: C 49.40; H 2.76; N 16.46; S 18.84.

2-[5-Amino-6-cyano-7-(2-thienyl)-2-thioxo-3,7-dihydro-2*H*-pyrano[2,3-*d*][1,3]thiazol-3-ylamino]-*N*-phenyl-2-thioxoacetamide (VIIe). Yield 56% (*b*), yellow crystals, mp 167–168°C. ^{1}H NMR spectrum, δ, ppm: 5.2 s (1H, 7-H), 7.1–7.6 m (8H, H_{arom}), 11.1 s (2H, NH_2). ^{13}C NMR spectrum, δ_C, ppm: 33.57 (C^7); 59.60, 96.11, 139.99, 155.75 (C^{3a}, C^5, C^6, C^{7a}); 116.72 (CN); 121.73 (C^o); 124.11, 133.33 ($C^{3'}$, $C^{4'}$, $C^{5'}$); 125.88 (C^p); 132.25 (C^m); 140.92 ($C^{2'}$); 142.11 (C^i); 160.70 (C=O); 169.87, 187.77 (C=S). Mass spectrum, *m*/*z* (I_{rel}, %): 293 (37), 178 (45). Found, %: C 48.44; H 2.81; N 14.83; S 27.25. $C_{19}H_{13}N_5O_2S_4$. Calculated, %: C 48.39; H 2.78; N 14.85; S 27.20.

2-[5-Amino-6-cyano-7-(5-nitrofuran-2-yl)-2-thioxo-3,7-dihydro-2*H*-pyrano[2,3-*d*][1,3]thiazol-3-ylamino]-*N*-phenyl-2-thioxoacetamide (VIIf). Yield 59% (*b*), yellow crystals, mp 173–174°C. ^{1}H NMR spectrum, δ, ppm: 5.6 s (1H, 7-H), 7.1–7.65 m (8H, H_{arom}), 11.0 s (2H, NH_2). ^{13}C NMR spectrum, δ_C, ppm: 34.43 (C^7); 61.04, 93.52, 142.00, 156.93 (C^{3a}, C^5, C^6, C^{7a}); 105.11, 114.88 ($C^{3'}$, $C^{4'}$); 118.28 (CN); 121.74 (C^o); 125.88 (C^p); 132.25 (C^m); 140.99 (C^i); 160.90 (C=O); 169.97, 187.81 (C=S). Mass spectrum, *m*/*z* (I_{rel}, %): 321 (27), 178 (39). Found, %: C 45.63; H 2.43; N 16.82; S 19.19. $C_{19}H_{12}N_6O_5S_3$. Calculated, %: C 45.59; H 2.42; N 16.79; S 19.22.

2-(5-Amino-6-oxo-2-thioxo-3,11b-dihydro-2*H*,6*H*-chromeno[4′,3′:4,5]pyrano[2,3-*d*][1,3]thiazol-3-ylamino)-*N*-phenyl-2-thioxoacetamide (VIIIa). *a*. A mixture of 0.03 g (0.075 mmol) of compound **IIf**, 0.005 g (0.075 mmol) of malononitrile, and several drops of triethylamine in 7 ml of DMF was heated for 8 h under reflux. The product was purified by column chromatography using ethyl acetate–petroleum ether (1:3) as eluent. Yield 0.013 g (35%).

b. An ampule was charged with a mixture of 0.03 g (0.075 mmol) of 2-hydroxybenzylidenerhodanine **IIf** and 0.005 g (0.075 mmol) of malononitrile in 2 ml of acetic acid. The ampule was placed in a microwave oven and was irradiated for 1.5 h at a power of 210 W. The mixture was cooled and poured into water, and the precipitate was filtered off and recrystallized from aqueous ethanol. Yield 0.03 g (85%), bright yellow crystals, mp 176–177°C. ^{1}H NMR spectrum, δ, ppm: 5.35 s (1H, 11b-H), 7.0–7.7 m (9H, H_{arom}), 9.7 s (1H, NH), 11.0 s (2H, NH_2). ^{13}C NMR spectrum, δ_C, ppm: 40.57 (C^{11b}); 82.44, 97.18, 144.52, 158.72 ($C_{hetaryl}$); 118.27, 121.73, 125.88, 127.33, 128.11, 132.25, 120.36, 141.20, 154.57 (C_{arom}); 160.37, 161.12 (C=O); 168.75, 187.23 (C=S). Mass spectrum, *m*/*z* (I_{rel}, %): 304 (25), 178 (58). Found, %: C 52.31; H 2.90; N 11.65;

S 19.90. $C_{21}H_{14}N_4O_4S_3$. Calculated, %: C 52.27; H 2.92; N 11.61; S 19.93.

Compounds **VIIIb** and **VIIIc** were synthesized in a similar way.

2-(5-Amino-6-oxo-2-thioxo-3,11b-dihydro-2*H*,6*H*-chromeno[4′,3′:4,5]pyrano[2,3-*d*][1,3]thiazol-3-ylamino)-*N*-(4-chlorophenyl)-2-thioxoacetamide (VIIIb). Yield 83% (*b*), yellow crystals, mp 176–177°C. ^{1}H NMR spectrum, δ, ppm: 5.3 s (1H, 11b-H), 7.0–7.6 m (8H, H_{arom}), 9.6 s (1H, NH), 10.9 s (2H, NH_2). ^{13}C NMR spectrum, δ_C, ppm: 40.58 (C^{11b}); 82.44, 97.19, 144.53, 158.72 ($C_{hetaryl}$); 118.26, 121.23, 127.27, 128.04, 129.60, 120.37, 130.63, 138.85, 154.55 (C_{arom}); 160.38, 161.14 (C=O); 168.87, 187.34 (C=S). Mass spectrum, *m*/*z* (I_{rel}, %): 304 (34), 214 (47). Found, %: C 48.84; H 2.50; Cl 6.81; N 10.87; S 18.58. $C_{21}H_{13}ClN_4O_4S_3$. Calculated, %: C 48.79; H 2.53; Cl 6.86; N 10.84; S 18.61.

2-(5-Amino-6-oxo-2-thioxo-3,11b-dihydro-2*H*,6*H*-chromeno[4′,3′:4,5]pyrano[2,3-*d*][1,3]thiazol-3-ylamino)-*N*-(4-methoxyphenyl)-2-thioxoacetamide (VIIIc). Yield 80% (*b*), yellow crystals, mp 193–194°C. ^{1}H NMR spectrum, δ, ppm: 3.7 s (3H, OCH_3), 5.25 s (1H, 11b-H), 6.8–7.55 m (8H, H_{arom}), 9.4 s (1H, NH), 11.1 s (2H, NH_2). ^{13}C NMR spectrum, δ_C, ppm: 40.58 (C^{11b}); 55.48 (OCH_3); 82.45, 97.20, 144.52, 158.71 ($C_{hetaryl}$); 116.71, 118.27, 121.25, 127.30, 128.02, 120.35, 135.63, 154.57, 156.12 (C_{arom}); 160.37, 161.20 (C=O); 168.95, 187.37 (C=S). Mass spectrum, *m*/*z* (I_{rel}, %): 304 (34), 210 (77). Found, %: C 51.61; H 3.15; N 10.97; S 18.73. $C_{22}H_{16}N_4O_5S_3$. Calculated, %: C 51.55; H 3.15; N 10.93; S 18.77.

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