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SYNTHESIS AND ALKYLATION OF NEW DERIVATIVES OF CONDENSED THIENO[3,2-*d*]PYRIMIDINE-8,10-DITHIONES

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The Thorpe-Ziegler reaction has been carried out. Condensed 1-amino-2-substituted-thieno[2,3-*b*]pyridines were obtained from cyanopyridinethiones and halogen-containing compounds. Synthesized derivatives of 8-imino-pyrido- [3',2':4,5]thieno[3,2-*d*][1,3]thiazine-10-thiones with carbon disulfide in the presence of absolute pyridine were further recyclized with Dimroth rearrangement to obtain new derivatives of condensed thieno[3,2-*d*]-pyrimidine-8,10-dithiones. The thieno[3,2-*d*]pyrimidine-8,10-dithiones were alkylated with various alkyl halides to afford *S*-alkyl derivatives. The structures of newly synthesized compounds were confirmed by IR, ^{1}H NMR, MS spectral data and elemental analysis.

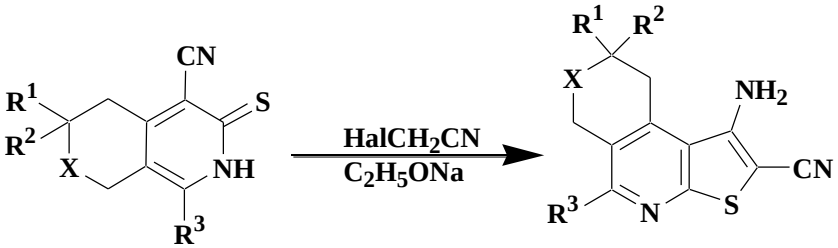
References 21.

Synthetic thiophenes have been reported to possess a wide range of therapeutic properties with diverse applications in medicinal chemistry and material science, attracting great interest in both industryand academia [1]. Pyridine and pyrimidine derivatives are known to form the basis of many medications. Pyrimidines and fused pyrimidines, being integral parts of DNA and RNA, play an essential role in several biological processes and also have considerable chemical and pharmacological importance as antibiotics, antibacterials, cardiovascular as well as agrochemical and veterinary products [1-4]. Heterocyclic compounds play an important role in designing new classes of structural entities of medicinal importance with potentially new mechanisms of action. In addition, during the last few years, condensed thienopyrimidine

derivatives have received considerable attention. Many of these derivatives were found to possess a variety of pronounced activities such as anti-inflammatory and analgesic [5-8], antimicrobial [9-13], anti-Avian influenza virus (H5N1) [14], anti-herpes simplex virus type 1 (HSV-1) and hepatitis-A virus (HAV), serotonin 5-HT6 receptor antagonist [15], antiarrhythmic [16] agent. Pyrimidine derivatives have been previously reported as platelet aggregation inhibitors, antagonists, anti-conceptive and anti-parkinsonism [17-20] agents. Heterocyclic compounds have also exhibited anthelmintic, anti HIV and hypoglycemic activities [21]. Therefore, obtaining new derivatives of these heterocycles to a great extent is a guarantee for revealing biological activity in synthesized compounds. In view of these observations and as continuation of our previous works on heterocyclic chemistry, we report herein the synthesis of some new heterocycle-containing pyridothienopyrimidine moieties and their chemical properties.

The synthesis of condensed 1-amino-2-substituted-thieno[2,3-*b*]pyridines (**2**) from 5-cyanopyridine-6-thiones (**1**) and halogen-containing compounds having the electron-withdrawing nitrile group in the *α*-position was carried out by the Thorpe-Ziegler reaction under the influence of sodium alkoxide (Scheme 1).

Scheme 1

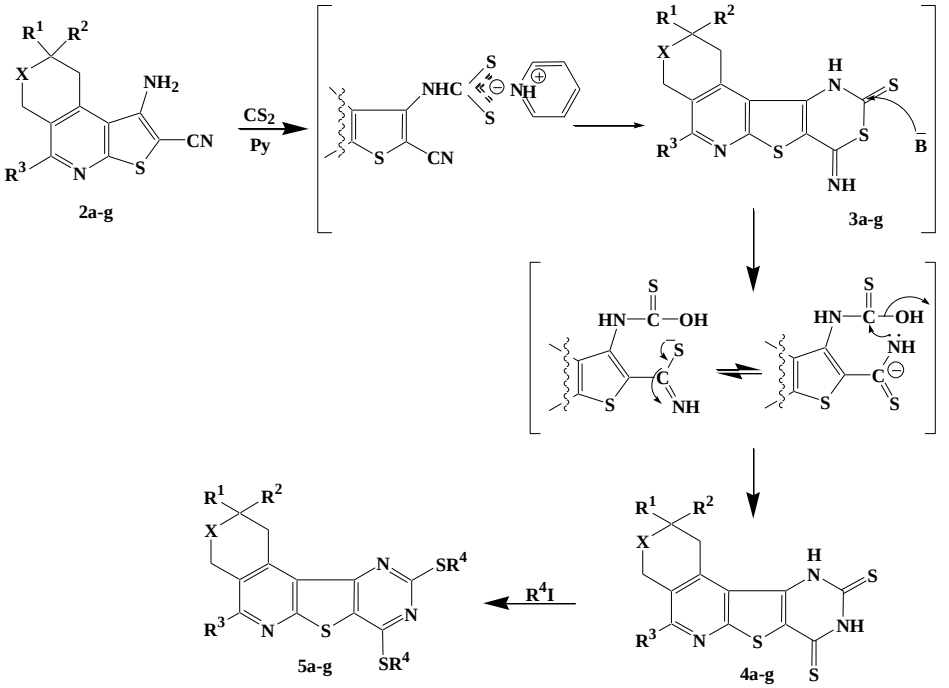


1a-g **2a-g**

1,2 a-b: X = CH_2, $R^1 = R^2 = H$; **1,2 c:** X = NCH_3, $R^1 = R^2 = H$;
1,2 d: X = O, $R^1 = H$, $R^2 = i\text{-}C_3H_7$; **1,2 g:** X = S, $R^1 = R^2 = H$;
1,2e,f: X = O, $R^1 = R^2 = CH_3$, **1,2a:** R^3 = pyrrolidil;
1,2b-e,g: R^3 = morpholyl; **1,2f:** R^3 = piperidyl.

By the interaction of 1-amino-2-cyano derivatives of thieno[2,3-*b*]pyridines (**2**) with carbon disulfide in a pyridine medium, we synthesized new derivatives of fused thieno[3,2-*d*]pyrimidine-8,10-dithiones (**4**). Reaction proceeded with the formation of intermediate compounds **3** (Scheme 2). Then thieno[3,2-*d*]-1,3-thiazines (**3**), an interesting example of rearrangement with Dimroth exchange and transformation observed under the action of alkali, were subjected to recycling, which led to the formation of reaction products. Intermediate product **3** was isolated, the structure of which was proved by the methods of NMR- and IR-spectroscopy and mass-spectrometry.

Scheme 2



2,3,4,5 a-b: X = CH_2, $R^1 = R^2 = H$; **2,3,4 c:** X = NCH_3, $R^1 = R^2 = H$;
2,3,4,5 d, 5 c: X = O, $R^1 = H$, $R^2 = i\text{-}C_3H_7$; **2,3,4 g:** X = S, $R^1 = R^2 = H$;
2,3,4,5 e,f, 5 g: X = O, $R^1 = R^2 = CH_3$, **2,3,4,5 a:** R^3 = pyrrolidil;
2,3,4 b-e,g, 5 b,d,e: R^3 = morpholyl; **2,3,4,5 f, 5 g:** R^3 = piperidyl;
5 a-c,e,f: $R^4 = CH_3$, **5 d,g:** $R^4 = C_2H_5$.

The signals of two NH group protons were observed in ^1H NMR spectra at ranges of 11.20 and 12.59 ppm, correspondingly, and in the IR spectra, the absence of an absorption signal for the C=NH group proved the structures of the synthesized compounds **4**. In continuation of this work, the corresponding S-alkyl derivatives were synthesized by the alkylation of compounds 4 by alkyl halides.

Experimental section

All chemicals, reagents, and solvents were of commercially high purity grade purchased from Sigma-Aldrich. Melting points (mp.) were determined on a Boetius microtable. They are expressed in degree centigrade (ºC). ^1H NMR spectra were recorded with a Varian Mercury 300VX spectrometer in DMSO-d_6:CCl_4 (1:3) at 300 *MHz* (^1H). Chemical shifts were reported as ppm (parts per million) relative to TMS (tetramethylsilane) as the internal standard. IR spectra were recorded on Nicolet Avatar 330-FTIR spectrophotometer and the reported wave numbers are given in cm^{-1}. TLC analyses were performed on Silufol UV-

254 plates using pyridine–ethyl acetate, 2:1, acetone–hexane, 1:1 as eluent; spots were developed with iodine vapor.

General procedure for the synthesis of thieno[2,3-*b*]pyridines 2a-b. A mixture of 0.01 *mol* of 5-cyanopyridinethiones **1** and 0.01 *mol* of chloroacetonitrile was added to sodium ethoxide solution obtained from 0.46 *g* (0.02 *mol*) of sodium metal and 50 *ml* of anhydrous ethanol. The reaction mixture was refluxed at 60°C for 2 *h*. The solution was cooled, 50 *ml* of cold water was added. The obtained precipitate was filtered off, washed with water, and dried. Recrystallized from ethanol.

1-Amino-5-pyrrolidin-1-yl-6,7,8,9-tetrahydrothieno[2,3-*c*]isoquinoline-2-carbonitrile (2a). Yield 2.3 *g* (78.3%), mp 232-236°C, R_f 0.48. Found, %: C 64.68; H 6.16; N 18.58; S 10.81. $C_{16}H_{18}N_4S$. Calculated, %: C 64.40; H 6.08; N 18.78; S 10.75. IR spectrum, *v*, cm^{-1}: 3480-3400 (NH_2); 2200 (CN); 1620 (C=O); 1600-1590 ($C=C_{Ar}$).^{1}H NMR spectrum, δ, ppm, MHz: 1.70-1.84 m (4H, $2CH_2$); 1.90-1.92 m (4- H, $(CH_2)_2$); 2.63 t (2 H, *J* = 5.6, CH_2); 3.21 t (2 H, *J* = 6.4, CH_2); 3.51-3.53 m (4 H, $N(CH_2)_2$); 5.69 s (2 H, NH_2).

1-Amino-7-methyl-5-morpholin-4-yl-6,7,8,9-tetrahydrothieno[2,3-*c*]-2,7-naphthyridine-2-carbonitrile (2c). Yield 2.3 *g* (74.1%), mp 270-271°C, R_f 0.68. Found, %: C 60.59; H 6.56; N 19.45; S 8.80. $C_{18}H_{23}N_5OS$. Calculated, %: C 60.48; H 6.49; N 19.59; S 8.97. IR spectrum, *v*, cm^{-1}: 3490-3400 (NH_2); 2200 (CN); 1630 (C=O); 1600-1580 ($C=C_{Ar}$). ^{1}H NMR spectrum, δ, ppm, MHz: 1.12 s (6H, $2CH_3$);2.10 s (3H, CH_3); 2.31 s (2H, 9-CH_2); 3.00-3.21 m (4H, $N(CH_2)_2$); 3.52 s (2 H, 6-CH_2); 3.61-3.80 m (4H, $O(CH_2)_2$); 6.33 s (2H, NH_2).

1-Amino-8-isopropyl-5-morpholin-4-yl-8,9-dihydro-6*H*-pyrano[4,3-*d*]thieno-[2,3-*b*]pyridine-2-carbonitrile (2d). Yield 2 *g* (56.5%), mp 264-265°C, R_f 0.54. Found, %: C 60.18; H 6.26; N 15.48; S 8.79. $C_{18}H_{22}N_4O_2S$. Calculated, %: C 60.31; H 6.19; N 15.63; S 8.95. ^{1}H NMR spectrum,δ, ppm, MHz: 1.02 d (3 H, *J* = 3.9, CH_3); 1.04 d (3 H, *J* = 4.7, CH_3); 1.80 okt (1 H, *J* = 6.2, CH); 3.02-3.37 m (7 H, CH_2, $N(CH_2)_2$ and OCH); 3.66-3.82 m (4 H, $O(CH_2)_2$); 4.59 d (1 H, *J* = 14.7) and 4.74 d (1 H, *J* = 14.3, OCH_2); 5.96 s (2 H, NH_2).

1-Amino-8,8-dimethyl-5-piperidin-1-yl-8,9-dihydro-6*H*-pyrano[4,3-*d*]thieno-[2,3-*b*]pyridine-2-carbonitrile (2f). Yield 2.5 *g* (74.9%), mp 238-239°C, R_f 0.58. Found, %: C 63.38; H 6.61; N 16.48; S 9.49. $C_{18}H_{22}N_4OS$. Calculated, %: C 63.13; H 6.47; N 16.36; S 9.36. ^{1}H NMR spectrum, δ, ppm, MHz: 1.30 s (6 H, $2CH_3$); 1.67-1.71 m (6 H, $3CH_2$); 3.08 s (2 H, CH_2); 3.11-3.18 m (4 H, $N(CH_2)_2$); 4.57 s (2 H, OCH_2); 5.91 s (2 H, NH_2).

1-Amino-8,8-dimethyl-5-morpholin-4-yl-8,9-dihydro-6*H*-thieno[2,3-*b*]thiopy-rano[4,3-*d*]pyridine-2-carbonitrile (2g). Yield 2.9 *g* (80.0%), mp 241-242°C, R_f 0.67. Found, %: C 56.73; H 6.06; N 15.46; S 17.64. $C_{17}H_{20}N_4OS_2$. Calculated, %: C 56.64; H 5.59; N 15.54; S 17.79. IR spectrum, *v*, cm^{-1}: 3490-3400 (NH_2); 2220 (CN); 1630 (C=O), 1600-1580 ($C=C_{Ar}$). ^{1}H NMR spectrum,

δ, ppm, MHz: 1.37 s (6 H, $2CH_3$); 3.04-3.38 m (6 H, $3CH_2$); 3.65-3.97 m (6 H, $3CH_2$); 6.48 s (2 H, NH_2).

The preparation of compound **2b, e** is given in [4].

General method for the synthesis of compounds 3b, c, e, g. A mixture of 0.01 *mol* of compound **2**, 9 *ml* of carbon disulfide and 15 *ml* of absolute pyridine was refluxed for 10 *h*. After cooling, the crystals were filtered, washed with water and dried. Recrystallized from DMF.

8-Imino-5-morpholin-4-yl-1,2,3,4,8,11-hexahydro-10*H*-[1,3]thiazino-[4',5':4,5] thieno[2,3-*c*]isoquinoline-10-thione (3b). Yield 3.7 *g* (95.2%), mp >360 °C, R_f 0.62. Found, %: C 52.41; H 4.56; N 14.26; S 24.81. $C_{17}H_{18}N_4OS_3$. Calculated, %: C 52.28;H 4.65; N 14.35; S 24.63. IR spectrum, *v*, cm^{-1}: 3450, 3130 (NH); 1650 (C=N), 1580 ($C=C_{Ar}$), 1150 (C=S). Mass spectrum, m/z ($I_{rel, \%}$): 390 [M^+] (100), 359 (33), 345 (34), 333 (40), 305 (10).

8-Imino-2,2,3-trimethyl-5-morpholin-4-yl-1,2,3,4,8,11-hexahydro-10*H*-[1,3]-thiazino[4',5':4,5]thieno[2,3-*c*]-2,7-naphthyridine-10-thione (3c). Yield 3.4 *g* (78.9%), mp 315-316°C, R_f 0.59. Found, %: C 52.51; H 5.47; N 16.06; S 22.30. $C_{19}H_{23}N_5OS_3$. Calculated, %: C 52.63; H 5.35; N 16.15; S 22.19. IR spectrum, *v*, cm^{-1}: 3450, 3120 (NH); 1630 (C=N), 1580 ($C=C_{Ar}$), 1180 (C=S). ^{1}H NMR spectrum, δ, ppm, MHz: 1.16 s (6H, $2CH_3$); 2.12 s (3H, CH_3); 2.33 s (2H, 9-CH_2); 3.10-3.28 m (4H, $(CH_2)_2$); 3.52 s (2 H, 6-CH_2); 3.61-3.80 m (4H, $O(CH_2)_2$); 10.33 br (1H, NH). 13.18 br (1H, NH).

8-Imino-2,2-dimethyl-5-morpholin-4-yl-1,4,8,11-tetrahydro-2*H*,10*H*-pyrano-[4'',3'':4',5']pyrido[3',2':4,5]thieno[3,2-*d*][1,3]thiazine-10-thione (3e). Yield 2.9 *g* (70.0%), mp >360°C, R_f 0.68. Found, %: C 51.29; H 4.86; N 13.43; S 23.00. $C_{18}H_{20}N_4O_2S_3$. Calculated, %: C 51.40; H 4.79; N 13.32; S 22.87. IR spectrum, *v*, cm^{-1}: 3405, 3100 (NH); 1650 (C=N), 1590 ($C=C_{Ar}$), 1150 (C=S). Mass spectrum, m/z ($I_{rel, \%}$): 423 [M^+] (43), 405 (5), 389 (7), 363 (8), 344 (100), 329 (7), 313 (20). ^{1}H NMR spectrum, δ, ppm, MHz: 1.31 s (6 H, $2CH_3$); 3.08 t (4 H, *J* = 1.5, $N(CH_2)_2$); 3.65 ddd (2H, *J* = 13.2, 4.5, 1.0) and 3.70 ddd (2 H, *J* = 13.2, 4.5, 0.9, $O(CH_2)_2$); 3.80 s (2 H, CH_2); 5.23-5.32 m (2 H, OCH_2); 10.18 br (2 H, NH, C=NH).

8-Imino-2,2-dimethyl-5-morpholin-4-yl-1,4,8,11-tetrahydro-2*H*,10*H*-thiopyra-no[4'',3'':4',5']pyrido[3',2':4,5]thieno[3,2-*d*][1,3]thiazine-10-thione (3g). Yield 3.6 *g* (82.7%), mp >360 °C, R_f 0.70. Found, %: C 49.39; H 4.71; N 12.97; S 29.25. $C_{18}H_{20}N_4OS_4$. Calculated, %: C 49.51; H 4.62; N 12.83; S 29.38. IR spectrum, *v*, cm^{-1}: 3420, 3130 (NH); 1630 (C=N), 1570 ($C=C_{Ar}$), 1140 (C=S). ^{1}H NMR spectrum, δ, ppm, MHz: 1.26 s (6 H, $2CH_3$); 3.35-3.38 m (6 H, $N(CH_2)_2$); 3.65-3.80 m (6 H, $O(CH_2)_2$); 5.18-5.32 m (2 H, OCH_2); 3.89 t (2 H, *J* = 2.1, SCH_2); 10.18 br.s (1 H, NH); 13.55 br (1H, NH).

Preparation of compounds 4a, d, f (General method). A mixture of 0.01 *mol* of compound **2** and 7.6 *g* (0.1 *mol*) of carbon disulfide in 15 ml of absolute pyridine was boiled for 10 *h*. The product formed after cooling was collected, crystals were filtered off and washed with alcohol.

5-Pyrrolidin-1-yl-1,2,3,4-tetrahydropyrimido[4',5':4,5]thieno[2,3-*c*]isoquino-line-8,10(9*H*,11*H*)-dithione (4a). Yield 1.8 *g* (47.8%), mp >360°C, R_f 0.48. Found, %: C 54.72; H 4.71; N 14.77; S 25.42. $C_{17}H_{18}N_4S_3$. Calculated, %: C 54.52; H 4.84; N 14.96; S 25.68. IR spectrum, *v*, cm^{-1}: 3400, 3360 (NH); 1560 (C=C_{Ar}), 1170 (C=S). ^{1}H NMR spectrum, δ, ppm, MHz: 1.72 m (2 H, 2-CH_2); 1.84 m (6 H, 3-CH_2, 2CH_2); 2.79 m (2 H, 4-CH_2); 3.39 m (2 H, 1-CH_2); 3.68 t (4 H, *J* = 3.1, N(CH_2)$_2$); 11.98 br.s (1 H, NH); 12.52 s (1 H, NH).

2-Isopropyl-5-morpholin-4-yl-1,4-dihydro-2*H*-pyrano[4'',3'':4',5']pyrido-[3',2':4,5]thieno[3,2-*d*]pyrimidine-8,10(9*H*,11*H*)-dithione (4d). Yield 3.5 *g* (80.7%), mp >360°C, R_f 0.55. Found, %: C 52.38; H 5.16; N 12.69; S 22.32. $C_{19}H_{22}N_4O_2S_3$. Calculated, %: C 52.51; H 5.10; N 12.89; S 22.13. IR spectrum, *v*, cm^{-1}: 3330, 3410 (NH); 1580 (C=Cap), 1150 (C=S). Mass spectrum, m/z ($I_{rel, \%}$): 434 [M^+] (5), 326 (20), 283 (5), 124 (20), 78 (15), 43 (29), 34 (56). ^{1}H NMR spectrum, δ, ppm, MHz: 1.03d (3 H, *J* = 6.7, CH_3); 1.07 d (3 H, *J* = 6.7, CH_3); 1.84 ok (1 H, *J* = 6.7, CH); 3.12 dd (*J* = 7.3, 10.2) and 3.63 ddd (2 H, *J* = 17.3, 4.0, 1.3, CH_2); 3.17-3.44 m (5 H, OCH, N(CH_2)$_2$); 3.70 ddd (2 H, *J* = 11.4, 6.5, 3.0) and 3.81 ddd (2 H, *J* = 11.4, 6.3, 3.0, O(CH_2)$_2$); 4.72 s (2 H, OCH_2); 11.20 br.s (1 H, NH); 12.59 br.s (1 H, NH).

2,2-Dimethyl-5-piperidin-1-yl-1,4-dihydro-2*H*-pyrano[4'',3'':4',5']pyrido-[3',2':4,5]thieno[3,2-*d*]pyrimidine-8,10(9*H*,11*H*)-dithione (4f). Yield 3.5 *g* (83.7%), mp >360°C, R_f 0.62. Found, %: C 54.34; H 5.16; N 13.71; S 22.72. $C_{19}H_{22}N_4OS_3$. Calculated, %: C 54.52; H 5.30; N 13.38; S 22.98. IR spectrum, *v*, cm^{-1}: 3580, 3410 (NH); 1570 (C=C_{Ar}), 1180 (C=S). Mass spectrum, m/z ($I_{rel, \%}$): 418 [M^+] (5), 385 (13), 187 (20), 186 (7), 80 (25), 46 (45), 32 (15). ^{1}H NMR spectrum, δ, ppm, MHz: 1.38 s (6 H, 2CH_3); 1.79 s (6 H, 3CH_2); 3.21 t (4 H, *J* = 3.6, N(CH_2)$_2$); 3.38 s (2 H, CH_2); 4.68 s (2 H, OCH_2); 11.62 br.s (1 H, NH); 12.21 s (1 H, NH).

Preparation of compounds 4b, c, e, g (General method). A mixture of 0.01 *mol* of compound **2**, 30 *ml* of a 5% potassium hydroxide solution was heated on a boiling water bath for 1 *h*. After cooling, the resulting solution was acidified with acetic acid, the precipitated crystals were filtered off, washed with water and dried. Recrystallized from nitromethane.

5-Morpholin-4-yl-1,2,3,4-tetrahydropyrimido[4',5':4,5]thieno[2,3-*c*]isoquino-line-8,10(9*H*,11*H*)-dithione (4b). Yield 76.9%, mp >360°C, R_f 0.59. Found, %: C 52.12; H 4.78; N 14.47; S 24.52. $C_{17}H_{18}N_4OS_3$. Calculated, %: C 54.28; H 4.65; N 14.35; S 24.63. IR spectrum, *v*, cm^{-1}: 3400, 3310 (NH); 1560 (C=C_{Ar}), 1130 (C=S). ^{1}H NMR spectrum, δ, ppm, MHz: 1.63-1.81 m (4H, 2CH_2); 2.58-2.72 m (4H, 2CH_2); 3.25-3.79 m (8H, 4CH_2); 11.67 br.s (1 H, NH); 12.10 br (1H, NH).

2,2,3-Trimethyl-5-morpholin-4-yl-1,2,3,4-tetrahydropyrimi-do[4',5':4,5]thieno-[2,3-*c*]-2,7-naphthyridine-8,10(9*H*,11*H*)-dithione (4c). Yield 80.8%, mp 285-286°C, R_f 0.74. Found, %: C 52.79; H 5.23; N 16.32; S 22.04. $C_{19}H_{23}N_5OS_3$. Calculated, %: C 52.63; H 5.35; N 16.15; S 22.19. IR

spectrum, *v*, cm^{-1}: 3380, 3290 (NH); 1590 (C=C_{Ar}), 1120 (C=S). ^{1}H NMR spectrum, δ, ppm, MHz: 1.16 s (6H, $2CH_3$); 2.09 s (3H, CH_3); 2.30 s (2H, 9-CH_2); 3.12-3.23 m (4H, $N(CH_2)_2$); 3.53 s (2 H, 6-CH_2); 3.60-3.80 m (4H, $O(CH_2)_2$); 11.28 br (1H, NH); 12.25 br (1H, NH).

2,2-Dimethyl-5-morpholin-4-yl-1,4-dihydro-2*H*-pyrano[4'',3'':4',5'] pyrido-[3',2':4,5]thieno[3,2-*d*]pyrimidine-8,10(9*H*,11*H*)-dithione (4e). Yield (85.7%), mp >360 °C, R_f 0.71. Found, %: C 51.32; H 4.86; N 13.23; S 23.01 $C_{18}H_{20}N_4O_2S_3$. Calculated, %: C 51.40; H 4.79; N 13.32; S 22.87. IR spectrum, *v*, cm^{-1}: 3330, 3410 (NH), 1580 (C=C_{Ar}), 1150 (C=S). Mass spectrum, m/z ($I_{rel,\ \%}$): 420 [M^+] (I00), 405 (I0), 389 (16), 377 (8), 363 (25), 362 (33), 350 (35). ^{1}H NMR spectrum, δ, ppm, MHz: 1.30 s (6 H, $2CH_3$); 3.08 t (4H, *J* = 1.5, $N(CH_2)_2$); 3.71 ddd (2 H, *J* = 13.2, 3.5, 0.8) and 3.80 ddd (2 H, *J* = 13.2, 3.5, 0.9, $O(CH_2)_2$); 3.80-3.89 m (2 H, CH_2); 5.18-5.32 m (2 H, OCH_2); 11.67 br.s (1H, NH); 12.23 s (1 H, NH).

2,2-Dimethyl-5-morpholin-4-yl-1,4-dihydro-2*H*-thiopyrano[4'',3'':4', 5']-pyrido[3',2':4,5]thieno[3,2-*d*]pyrimidine-8,10(9*H*,11*H*)-dithione (4g). Yield 1.8 *g* (74.6%), mp >360°C, R_f 0.69. Found, %: C 49.42; H 4.53; N 12.72; S 29.29. $C_{18}H_{20}N_4OS_4$. Calculated, %: C 49.51; H 4.62; N 12.83; S 29.38. IR spectrum, *v*, cm^{-1}: 3400, 3320 (NH), 1590 (C=C_{Ar}), 1140 (C=S). ^{1}H NMR spectrum, δ, ppm, *MHz*: 1.24 s (6 H, $2CH_3$); 3.21-3.38 m (4H, $N(CH_2)_2$); 3.59-3.75 m (4H, $O(CH_2)_2$); 3.82-3.98 m (2 H, CH_2); 5.81-5.93 m (2 H, SCH_2); 11.35 br (1H, NH); 12.27 br (1H, 1NH).

General procedure for alkylation of compounds 5a-g: To a sodium methylate solution prepared from 0.46 *g* (0.02 *mol*) of sodium and 15 *ml* of methanol, 0.01 *mol* of pyridinethione **4** was added. Then, 2.84 *g* (0.02 *mol*) of methyl iodide (or EtI) was added dropwise with stirring. The mixture was stirred at 60°C for 5 *h*, cooled and diluted with 50 *ml* of water. The precipitated crystals were filtered off, washed with water, dried, and recrystallized from methanol.

8,10-Bis(methylthio)-5-pyrrolidin-1-yl-1,2,3,4-tetrahydropyrimido-[4',5':4,5]-thieno[2,3-*c*]isoquinoline (5a). Yield 3.5 *g* (87.0%), mp 215-217°C, R_f 0.45. Found, %: C 56.38; H 5.64; N 13.77; S 23.74. $C_{19}H_{22}N_4S_3$. Calculated, %: C 56.69; H 5.51; N 13.92; S 23.89. ^{1}H NMR spectrum, δ, ppm, MHz: 1.78 m (2 H, 2-CH_2); 1.82 m (2 H, 3-CH_2); 1.98 m (4 H, $2CH_2$); 2.61-2.79 m (8 H, 4-CH_2, $2SCH_3$); 3.48 t (4 H, *J* = 3.0, $N(CH_2)_2$); 3.78 m (2H, 1-CH_2).

8,10-Bis(methylthio)-5-morpholin-4-yl-1,2,3,4-tetrahydropyrimi-do[4',5':4,5]-thieno[2,3-*c*]isoquinoline (5b). Yield 3.8 *g* (89.5%), mp 204-205°C, R_f 0.65. Found, %: C 54.60; H 5.46; N 13.45; S 23.09. $C_{19}H_{22}N_4OS_3$. Calculated, %: C 54.52; H 5.30; N 13.38; S 22.98. ^{1}H NMR spectrum, δ, ppm, MHz: 1.65-2.05 m (4H, $2CH_2$); 2.55-2.82 m (8H, $2SCH_3$, CH_2); 3.18-4.01 m (10H, $5CH_2$).

2-Isopropyl-8,10-bis(methylthio)-5-morpholin-4-yl-1,4-dihydro-2*H*-pyrano-[4'',3'':4',5']pyrido[3',2':4,5]thieno[3,2-*d*]pyrimidine (5c). Yield 4.5 *g* (97.2%), mp 220-223°C, R_f 0.52. Found, %: C 54.74; H 5.82; N 12.34; S

20.56. $C_{21}H_{26}N_4O_2S_3$. Calculated, %: C 54.52; H 5.66; N 12.11; S 20.79. ^{1}H NMR spectrum, δ, ppm, MHz: 1.03 d (3 H, *J* = 6.7, CH_3); 1.06 d (3 H, *J* = 6.0, CH_3); 1.83 ok (1 H, *J* = 6.7, CH); 2.60 s (3 H, SCH_3); 2.74 s (3 H, SCH_3); 3.12-3.42 m (6 H, CH_2, $N(CH_2)_2$); 3.71-3.95 m (5 H, OCH, $O(CH_2)_2$); 4.68 d (1 H, *J* = 14.7) and 4.71 d (1 H, *J* = 14.0, OCH_2).

8,10-Bis(ethylthio)-2-isopropyl-5-morpholin-4-yl-1,4-dihydro-2*H*-pyrano-[4'',3'':4',5']pyrido[3',2':4,5]thieno[3,2-*d*]pyrimidine (5d). Yield 3.7 *g* (75.2%), mp 190-192°C, R_f 0.46. Found, %: C 56.48; H 6.34; N 11.34; S 19.26. $C_{23}H_{30}N_4O_2S_3$. Calculated, %: C 56.30; H 6.16; N 11.42; S 19.60. ^{1}H NMR spectrum, δ, ppm, MHz: 1.03-1.07 m (6 H, $2CH_3$); 1.42-1.46 m (6 H, $2SCH_2\underline{CH_3}$); 1.84 ok (1 H, *J* = 6.0, CH); 3.15-3.41 m (10 H, CH_2, $2S\underline{CH_2}CH_3$, $N(CH_2)_2$); 3.69-3.86 m (5 H, OCH, $O(CH_2)_2$); 4.69 d (1 H, *J* = 14.6) and 4.72 d (1 H, *J* = 13.7, OCH_2).

2,2-Dimethyl-8,10-bis(methylthio)-5-morpholin-4-yl-1,4-dihydro-2*H*-pyrano-[4'',3'':4',5']pyrido[3',2':4,5]thieno[3,2-*d*]pyrimidine (5e). Yield 3.6 *g* (94.1%), mp 256-257 °C, R_f 0.58. Found, %: C 53.67; H 5.30; N 12.57; S 21.35. $C_{20}H_{24}N_4O_2S_3$. Calculated, %: C 53.54; H 5.39; N 12.49; S 21.44. IR spectrum, *ν*, cm^{-1}: 1570 ($C=C_{Ar}$). ^{1}H NMR spectrum, δ, ppm, MHz: 1.28 s (6 H, $2CH_3$); 2.60 s (3 H, SCH_3); 2.76 s (3 H, SCH_3); 3.23 m (4 H, $N(CH_2)_2$); 3.22-3.40 m (6 H, CH_2, $N(CH_2)_2$); 3.71-3.95 m (5 H, $O(CH_2)_2$); 4.65 s (2 H, OCH_2).

2,2-Dimethyl-8,10-bis(methylthio)-5-piperidin-1-yl-1,4-dihydro-2*H*-pyrano-[4'',3'':4',5']pyrido[3',2':4,5]thieno[3,2-*d*]pyrimidine (5f). Yield 3.3 *g* (74.7%), mp 200-203 °C, R_f 0.54. Found, %: C 56.38; H 5.74; N 12.69; S 21.33. $C_{21}H_{26}N_4OS_3$. Calculated, %: C 56.47; H 5.87; N 12.54; S 21.53. ^{1}H NMR spectrum, δ, ppm, MHz: 1.29 s (6 H, $2CH_3$); 1.83-1.85 m (6 H, $3CH_2$); 2.61 s (3 H, SCH_3); 2.78 s (3 H, SCH_3); 3.20-3.23 m (4 H, $N(CH_2)_2$); 3.42 s (2 H, CH_2); 4.62 s (2 H, OCH_2).

8,10-Bis(ethylthio)-2,2-dimethyl-5-piperidin-1-yl-1,4-dihydro-2*H*-pyrano-[4'',3'':4',5']pyrido[3',2':4,5]thieno[3,2-*d*]pyrimidine (5g). Yield 2.9 *g* (62.5%), mp 172-175°C, R_f 0.62. Found, %: C 58.41; H 6.54; N 11.67; S 20.35. $C_{23}H_{30}N_4OS_3$. Calculated, %: C 58.20; H 6.37; N 11.80; S 20.26. ^{1}H NMR spectrum, δ, ppm, MHz: 1.28 s (6 H, $2CH_3$); 1.43 m (6 H, $2SCH_2\underline{CH_3}$); 1.83 m (6 H, $3CH_2$); 3.17-3.22 m (6 H, CH_2, $2S\underline{CH_2}CH_3$); 3.42 m (4 H, $N(CH_2)_2$); 4.62 s (2 H, OCH_2).

ԿՈՆԴԵՆՍՎԱԾ ԹԻԵՆՈ[3,2-d]ՊԻՐԻՄԻԴԻՆ-8,10-ԴԻԹԻՈՆՆԵՐԻ ՆՈՐ ԱՆՑՅԱԼՆԵՐԻ ՍԻՆԹԵԶԸ ԵՎ ԱԼԿԻԼԱՑՈՒՄԸ

Ե. Գ. ՊԱՐՈՆԻԿՅԱՆ, Ա. Ս. ՂԱՐՈՒԹՅՈՒՆՅԱՆ և Շ. Ֆ. ՂԱԿՈԲՅԱՆ

Կոնդենսված 1-ամինո-2-ցիանոթիենո[2,3-b]պիրրիդինների ստացման համար կիրառվել է Տորպ-Ցիգլերի ռեակցիան: 5-Ցիանոպիրրիդինթիոնները հիմնային միջավայրում ցիկլացվել են α-դիրքում ակտիվ մեթիլենային խումբ պարունակող հալոգենիդների հետ: Ստացված թիենոպիրրիդինները բացարձակ պիրրիդինի միջավայրում ծծմբաածխածնի հետ փոխազդեցության արդյունքում առաջացրել են 8-իմինոպիրրիդո[3',2':4,5]թիենո[3,2-

d][1,3]թիազին-10-թիոններ: Վերջիններս, ռեակցիոն միջավայրում ենթարկվելով Դիմրոտի վերախմբավորման, հանգեցրել են նոր կոնդեսված հետերոցիկլիկ համակարգերի՝ թիենո[3,2-d]-պիրիմիդին-8,10-դիթիոնների առաջացման: Ալկիլհալոգենիդներով 10-դիթիոնների նոր կոնդեսված հետերոցիկլիկ համակարգերի ալկիլացմամբ սինթեզվել են համապատասխան S-ալկիլածանցյալները:

СИНТЕЗ И АЛКИЛИРОВАНИЕ НОВЫХ ПРОИЗВОДНЫХ КОНДЕНСИРОВАННЫХ ТИЕНО[3,2-d]ПИРИМИДИН-8,10-ДИТИОНОВ

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Осуществлена реакция Торпа–Циглера. Из циапиридинтионов и галогенсодержащих соединений под действием алкоголятов щелочных металлов получены конденсированные 1-амино-2-замещенные тиено[2,3-*b*]пиридины. Синтезированы производные 8-имино-пиридо[3',2':4,5]тиено[3,2-*d*][1,3]тиазин-10-тионов с сероуглеродом в присутствии абсолютного пиридина, которые далее подвергнуты рециклизации с перегруппировкой Димрота, что приводит к образованию новых прозводных конденсированных тиено[3,2-*d*]пиримидин-8,10-дитионов. Разработан новый метод, который позволил исключить из реакционной среды пиридин и увеличить скорость циклизаций. Алкилированием тиено[3,2-*d*]-пиримидин-8,10-дитионов различными алкилгалогенидами синтезированы *S*-алкилпроизводные.

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