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SYNTHESIS AND TRANSFORMATIONS OF 3-ETHOXYCARBONYL-2-(N-R-THIOUREIDO)THIOPHENES

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3-Ethoxycarbonyl-2-(N-R-thioureido)-4,5,6,7-tetrahydrobenzo[b]thiophenes were obtained by the reaction of 2-amino-3-ethoxycarbonyl-4,5,6,7-tetrahydrobenzo[b]thiophene with isothiocyanates and of 3-ethoxycarbonyl-2-isothiocyanato-4,5,6,7-tetrahydrobenzo[b]thiophene with primary and secondary amines. The cyclization paths of the products leading to derivatives of thieno[2,3-d]pyrimidine and thieno[2,3-d]-1,3-thiazine were studied. The corresponding S-substituted derivatives were obtained by the alkylation of 3-R-2-thioxo-3,4,5,6,7,8-hexahydrobenzo[b]thieno[2,3-d]pyrimidin-4-ones.

Keywords: isothiocyanate, pyrimidine, thiazine, thiophene, alkylation, cyclization.

Compounds containing a condensed pyrimidine ring are of interest in the search for biologically active compounds [1-5]. It is known that the reaction of 2-amino-3-ethoxycarbonylthiophenes (**1**) [6] with isothiocyanates stops at the intermediate 3-ethoxycarbonyl-2-(N-R-thioureido)thiophenes (**2**) [1-3, 7, 8] (method A).

We have developed alternative paths for the synthesis of compounds **2**, involving the reaction of 3-ethoxycarbonyl-2-isothiocyanato-4,5,6,7-tetrahydrobenzo[*b*]thiophene (**3**) with primary and secondary amines of the aliphatic, aromatic, and heterocyclic series (method B) (Scheme 1). This method makes it possible to insert various types of substituents into the thiourea fragment of the products **2**, since the range of appropriate isothiocyanates is restricted (method A), and also to obtain compounds of type **4**.

2-(2-Benzothiazolylamino)-3-ethoxycarbonyl-4,5,6,7-tetrahydrobenzo[*b*]thiophene (**5**) was isolated when compound **3** was heated with *o*-aminothiophenol.

The cyclization of compounds **2** depends on the pH of the medium and leads to substances with various structures [7, 8]. Thus, when the thiophenes **2a-o** were heated in an alkaline medium the potassium salts of 3-R-mercapto-3,4,5,6,7,8-hexahydrobenzo[*b*]thieno[2,3-*d*]pyrimidin-4-ones **6a-o** were isolated, and their acidification gave compounds **6'a-g** respectively (Scheme 2). In an acidic medium compounds **2e**,**k** are converted into derivatives of 2-(R-amino)-4(H)-5,6,7,8-tetrahydrobenzo[*b*]thieno[2,3-*d*]-1,3-thiazin-4-one **7a**,**b** (Scheme 2).

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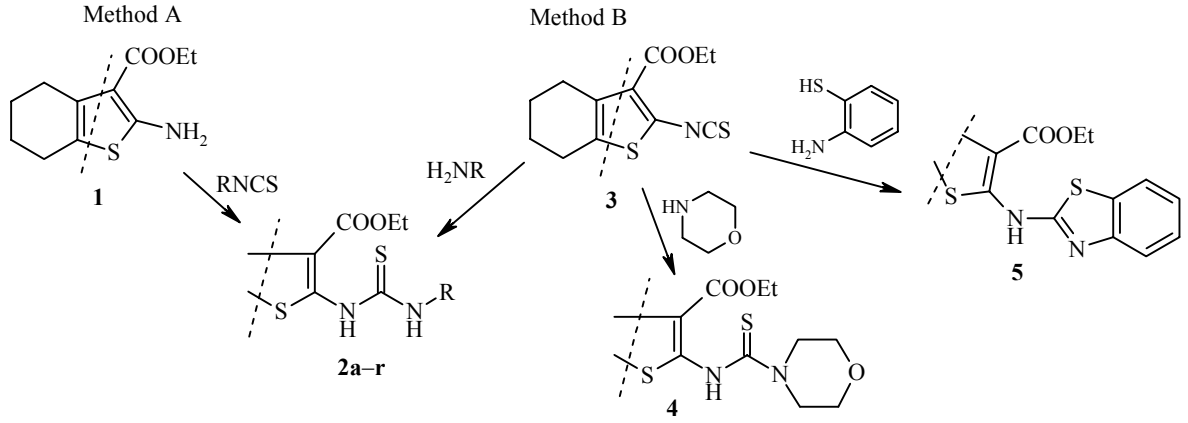
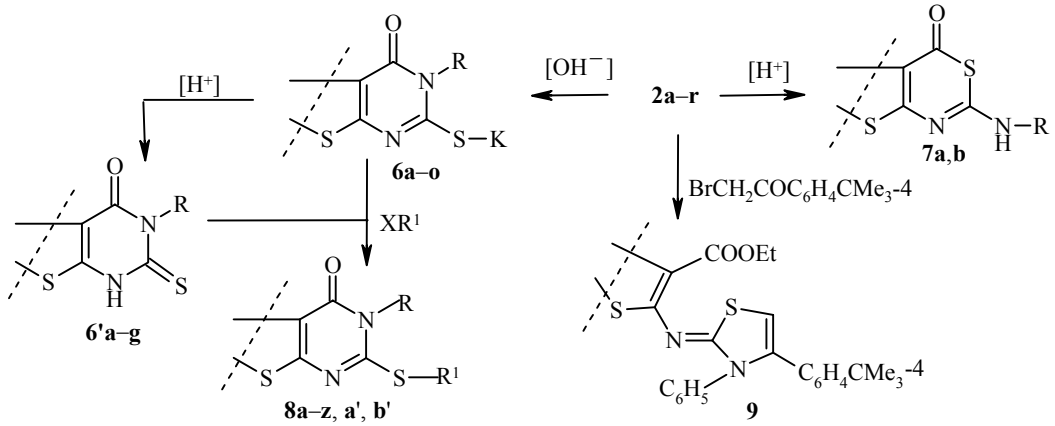
Scheme 1



2 a R = $CH_2CH=CH_2$; **b** R = Ph; **c** R = C_6H_4Me-4; **d** R = C_6H_4Me-2; **e** R = C_6H_4Br-4;
f R = $C_6H_3Cl_2$-2,4; **g** R = C_6H_4OMe-4; **h** R = C_6H_4OMe-2; **i** R = $C_6H_4OCHF_2$-4; **j** R = Bn;
k R = $C_6H_4NHCOMe$-4; **l** R = $N=CHC_6H_4F$-4; **m** R = 5-chloro-2-pyridyl; **n** R = 2,3-dimethyl-1-phenyl-5-oxo-4-pyrazolyl;
o R = 4,6-di(ethylamino)-1,3,5-triazin-2-ylamino; **p** R = C_6H_4OH-3; **q** R = NHPh; **r** R = $NHCOC_6H_4Br$-4

Compounds **6a-n** enter readily into reaction with alkylating reagents in an alkaline medium, and the corresponding S-substituted 3-R-2-alkyl(aryl)thio-3,4,5,6,7,8-hexahydrobenzo[*b*]thieno[2,3-*d*]pyrimidin-4-ones **8a-b'** are formed (Scheme 2). An attempt at a single-stage synthesis of substances with structure **8** by the

Scheme 2



6a R = $CH_2CH=CH_2$; **6'a**, **6b** R = Ph; **6c** R = C_6H_4Me-4; **6d** R = C_6H_4Me-2; **6e** R = C_6H_4Br-4; **6f** R = $C_6H_3Cl_2$-2,4;
6g, **6'b** R = C_6H_4OMe-4; **6h** R = C_6H_4OMe-2; **6i, 6'c** R = $C_6H_4OCHF_2$-4; **6j, 6'd** R = Bn; **6k** R = $C_6H_4NHCOMe$-4;
6l, 6'e R = $N=CHC_6H_4F$-4; **6m** R = 5-chloro-2-pyridyl; **6n**, **6'f** R = 2,3-dimethyl-1-phenyl-5-oxo-4-pyrazolyl;
6o, **6'g** R = 4,6-di(ethylamino)-1,3,5-triazin-2-ylamino; **7 a** R = C_6H_4Br-4; **b** R = $C_6H_4NHCOMe$-4; **8 a** R = $CH_2CH=CH_2$,
R^1 = CH_2COPh; **b** R = Ph, R^1 = CH_2COBu-*t*; **c** R = Ph; R^1 = $CH_2COC_6H_4Br$-4; **d** R = Ph, R^1 = $CH_2COC_6H_4OCHF_2$-2;
e R = Ph, R^1 = $CH_2COC_6H_4Ph$-4; **f** R = Ph, R^1 = $CH_2CONPhCHMe_2$; **g** R = C_6H_4Me-4, R^1 = CH_2COPh; **h** R = C_6H_4Me-2,
R^1 = $CH_2CONPhCHMe_2$; **i** R = C_6H_4Me-2, R^1 = Me; **j** R = C_6H_4Br-4, R^1 = $C_6H_3(NO_2)_2$-2,4; **k** R = C_6H_4Br-4, R^1 = $CH_2COC_6H_4Cl$-4;
l R = $C_6H_3Cl_2$-2,4, R^1 = $CH_2CONPhCHMe_2$; **m** R = C_6H_4OMe-2, R^1 = $CH_2COC_6H_4Br$-3; **n** R = C_6H_4OMe-4; R^1 = $CH_2COC_6H_4$-*t*-Bu-4;
o R = C_6H_4OMe-4, R^1 = $CH_2COC_6H_4Cl$-4; **p** R = $C_6H_4OCHF_2$-4, R^1 = $CH_2COC_6H_4F$-4; **q** R = $C_6H_4OCHF_2$-4, R^1 = $CH_2COC_6H_4Cl$-4;
r R = $C_6H_4OCHF_2$-4, R^1 = $CHMeCOC_6H_4Cl$-4; **s** R = $C_6H_4OCHF_2$-4, R^1 = $CH_2COC_6H_4OCHF_2$-4; **t** R = $C_6H_4OCHF_2$-4,
R^1 = $CH_2COC_6H_4(OCH_2)_2$-3,4; **u** R = Bn, R^1 = $CH_2COC_6H_4Cl$-4; **v** R = Bn, R^1 = $CH_2CONPhCHMe_2$; **w** R = $C_6H_4NHCOMe$-4,
R^1 = $C_6H_3(NO_2)_2$-2,4; **x** R = $C_6H_4NHCOMe$-4, R^1 = $CH_2COC_6H_4F$-4; **y** R = $C_6H_4NHCOMe$-4, R^1 = $CH_2CONPhCHMe_2$;
z R = $N=CHC_6H_4F$-4, R^1 = $CH_2CONPhCHMe_2$; **a'** R = 5-chloro-2-pyridyl; R^1 = $CH_2CONPhCHMe_2$;
b' R = 2,3-dimethyl-1-phenyl-5-oxo-4-pyrazolyl, R^1 = $C_6H_3(NO_2)_2$-2,4; X = Hal

TABLE 1. The Characteristics of Compounds **2a**-**r**, **4**, **5**, and **9**

Compound	Empirical formula	Found, % / Calculated, %		mp, °C	^{1}H NMR spectrum, δ, ppm (*J*, Hz)				Yield, %
		N	S		NH (s)	OCH_2 (q), CH_3 (t)	$(CH_2)_4$, (br. d, br. s)	R	
1	2	3	4	5	6	7	8	9	10
2a	$C_{15}H_{20}N_2O_2S_2$	8.48 / 8.64	19.54 / 19.75	148-149					82
2b	$C_{18}H_{20}N_2O_2S_2$	7.38 / 7.77	17.92 / 17.79	178-180	10.90; 11.80	4.23 (*J* = 7.2); 2.96 (*J* = 7.2)	2.65 (*J* = 35.8); 1.73	5.53-5.72 (5H, m, C_6H_5)	88
2c	$C_{19}H_{22}N_2O_2S_2$	7.10 / 7.49	16.86 / 17.11	175-176					89
2d	$C_{19}H_{22}N_2O_2S_2$	7.12 / 7.49	17.48 / 17.11	170-171					84
2e	$C_{18}H_{19}BrN_2O_2S_2$	6.08 / 6.38	14.22 / 14.58	182-183	11.10; 12.50	4.15 (*J* = 7.0); 1.20 (*J* = 7.0)	2.64 (*J* = 36.1); 1.71	7.90 (d, *J* = 8.7); 7.80 (4H, d, *J* = 8.7, C_6H_4)	86
2f	$C_{18}H_{18}Cl_2N_2O_2S_2$	6.36 / 6.52	14.62 / 14.93	157-158	10.90; 11.80	4.23 (*J* = 7.2); 1.29 (*J* = 7.2)	2.70 (*J* = 36.6); 1.71	7.76 (1H, s); 7.48-7.56 (2H, m, C_6H_3)	85
2g	$C_{19}H_{22}N_2O_3S_2$	6.84 / 7.17	16.62 / 16.42	163-164	10.60; 11.70	4.21 (*J* = 7.1); 1.25 (*J* = 7.1)	2.65 (*J* = 34.8); 1.71	7.31 (d, *J* = 8.9); 6.97 (4H, d, *J* = 8.9, C_6H_4); 3.77 (3H, s, OCH_3)	89
2h	$C_{19}H_{22}N_2O_3S_2$	7.42 / 7.17	16.08 / 16.42	161-162	10.60; 11.70	4.21 (*J* = 7.2); 1.25 (*J* = 7.2)	2.65 (*J* = 32.7); 1.71	6.96-7.81 (4H, m, C_6H_4); 3.78 (3H, s, OCH_3)	86
2i	$C_{19}H_{20}F_2N_2O_3S_2$	6.22 / 6.57	15.40 / 15.04	172-173	10.70; 11.80	4.22 (*J* = 7.1); 1.25 (*J* = 7.1)	2.65 (*J* = 30.5); 1.72	7.20-7.40 (5H, m, C_6H_4–$OCHF_2$-4)	89
2j	$C_{19}H_{22}N_2O_2S_2$	7.18 / 7.48	17.0 / 17.11	120-121	9.89; 11.60	4.26 (*J* = 7.2); 1.30 (*J* = 7.2)	2.65 (*J* = 39.3); 1.70	7.28-7.35 (5H, m, C_6H_5); 4.68 (2H, br. s, CH_2)	81

TABLE 1 (continued)

1	2	3	4	5	6	7	8	9	10
2k	$C_{20}H_{23}N_3O_3S_2$	10.42 / 10.07	15.65 / 15.34	203-204					81
2l	$C_{19}H_{20}FN_3O_2S_2$	10.26 / 10.37	16.10 / 15.80	230-231					68
2m	$C_{17}H_{18}ClN_3O_2S_2$	10.36 / 10.61	16.46 / 16.20	216-217	11.30; 15.20	4.32 (J = 7.2); 1.30 (J = 7.2)	2.67 (J = 33.3); 1.73	8.21 (d, J = 2.5); 7.94 (q, J = 8.7); 7.22 (d, J = 8.7, Py)	73
2n	$C_{23}H_{26}N_4O_3S_2$	12.12 / 11.90	14.0 / 13.63	211-212	9.77; 12.0	4.15 (J = 7.1); 1.23 (J = 7.1)	2.63 (J = 28.9); 1.70	7.39-7.52 (5H, m, C_6H_5); 3.32 (3H, s, NCH_3); 2.19 (3H, s, CH_3)	82.5
2o	$C_{19}H_{28}N_8O_2S_2$	24.38 / 24.12	13.56 / 13.80	191-192	10.12; 12.20	4.21 (J = 7.2); 1.19 (J = 7.0)	2.69 (J = 21.3); 1.70	8.86 (1H, s, NH); 8.66 (1H, s, NH); 7.00 (1H, s, NH); 3.45 (br. s); 1.06 (10H, br. s, Et_2)	67
2p	$C_{18}H_{20}N_2O_3S_2$	7.66 / 7.44	17.44 / 17.03	190-191	9.58; 10.80	4.22 (J = 7.2); 1.26 (J = 7.2)	2.63 (J = 33.9); 1.71	6.65-7.20 (4H, m, C_6H_4)	90.4
2q	$C_{18}H_{21}N_3O_2S_2$	11.52 / 11.20	17.44 / 17.07	193-194	10.30; 12.50	4.12 (J = 7.2); 1.17 (J = 7.2)	2.64 (J = 30.9); 1.70	8.34 (1H, s, NH); 6.80-7.40 (5H, m, C_6H_5)	56
2r	$C_{19}H_{20}BrN_3O_3S_2$	8.92 / 8.71	13.50 / 13.29	209-210	11.10; 12.50	4.15 (J = 7.2); 1.20 (J = 7.2)	2.64 (J = 29.4); 1.71	10.5 (1H, s, NH); 7.80 (d, J = 8.9); 7.90 (4H, d, J = 8.9, C_6H_4)	87
4	$C_{16}H_{22}N_2O_3S_2$	8.08 / 7.91	18.44 / 18.08	161-162	12.10	4.38 (J = 7.3); 1.31 (J = 7.3)	2.65 (J = 25.9); 1.72	3.74 (t, J = 9.2); 3.90 (8H, t, J = 9.2, $(CH_2)_4$)	98.8
5	$C_{18}H_{18}N_2O_2S_2$	7.62 / 7.82	18.06 / 17.88	131-132	11.36	4.30 (J = 7.2); 1.31 (J = 7.2)	2.67 (J = 20.7); 1.73	7.88 (4H, d, J = 11.1); 7.65 (d, J = 11.1); 7.39 (t, J = 11.1); 7.23 (4H, t, J = 11.1; 2-benzothiazolyl	95
9	$C_{30}H_{32}N_2O_2S_2 \cdot C_6H_3N_3O_7$	9.12 / 9.39	8.94 / 8.59	114-115	—	4.07 (J = 7.2); 1.11 (J = 7.2)	2.62 (br. s); 1.73	8.60 (2H, s, picric acid); 7.09-7.29 (9H, m, Ar); 6.75 (1H, s, CH); 1.20 (9H, s, t-Bu)	65

TABLE 2. The Characteristics of Compounds **6a**,**c-f**,**h**,**k**,**m**, **6'a**, and **7a**,**b**

Compound	Empirical formula	Found, % / Calculated, %		mp, °C	^{1}H NMR spectrum, δ, ppm (*J*, Hz)			Yield, %
		N	S		NH (s)	$(CH_2)_4$ (m; m)	R	
1	2	3	4	5	6	7	8	9
6a	$C_{13}H_{13}KN_2OS_2$	8.43 / 8.85	20.54 / 20.26	>300				95
6'a	$C_{16}H_{14}N_2OS_2$	7.86 / 8.91	20.70 / 20.39	276-277	13.70	2.76; 1.76	7.41-7.59 (5H, m, C_6H_5)	96
6c	$C_{17}H_{15}KN_2OS_2$	7.32 / 7.64	17.97 / 17.50	>300	—	2.72; 1.75	7.20 (d; *J* = 8.4); 7.40 (4H, d, *J* = 8.1, C_6H_4); 2.42 (3H, s, CH_3)	94
6d	$C_{17}H_{15}KN_2OS_2$	7.28 / 7.64	17.73 / 17.50	>300	—	2.77; 1.78	7.30 (4H, m, C_6H_4); 2.06 (3H, s, CH_3)	90
6e	$C_{16}H_{14}BrKN_2OS_2$	6.11 / 6.50	15.21 / 14.86	>300	—	2.77; 1.78	7.45 (d; *J* = 8.7); 7.80 (4H, d, *J* = 8.7; C_6H_4)	87
6f	$C_{16}H_{11}Cl_2KN_2OS_2$	6.32 / 6.65	15.47 / 15.22	>300	—	2.74; 1.76	7.67 (2H, s); 7.97 (1H, s, C_6H_3)	93
6'b	$C_{17}H_{16}N_2O_2S_2$	8.06 / 8.13	18.95 / 18.62	259-260	13.90	2.72; 1.75	7.34 (d, *J* = 8.7); 7.13 (4H, d, *J* = 8.7, C_6H_4); 3.85 (3H, s, OCH_3)	88
6h	$C_{17}H_{15}KN_2O_2S_2$	7.15 / 7.32	16.89 / 16.76	>300	—	2.70; 1.73	7.14-7.57 (4H, m, C_6H_4); 3.80 (3H, s, OCH_3)	92

TABLE 2 (continued)

1	2	3	4	5	6	7	8	9
6'c	$C_{17}H_{14}F_2N_2O_2S_2$	7.05 / 7.36	17.08 / 16.86	>300	13.70	2.68; 1.75	7.24-7.32 (5H, m, $C_6H_4OCHF_2$-4)	94
6'd	$C_{17}H_{16}N_2OS_2$	8.27 / 8.53	19.71 / 19.52	>300	13.69	2.70; 1.74	7.28-7.36 (5H, m, C_6H_5); 5.60 (2H, s, CH_2)	96
6k	$C_{18}H_{16}KN_3O_2S_2$	10.03 / 10.26	15.91 / 15.66	280-281	—	2.64; 1.76	9.91 (1H, s, NH); 7.50 (d, *J* = 8.8); 6.86 (4H, d, *J* = 8.8, C_6H_4); 2.06 (3H, s, CH_3)	93
6'l	$C_{17}H_{14}FN_3OS_2$	11.38 / 11.69	17.97 / 17.83	>300	14.00	2.75; 1.76	9.20 (1H, s, CH); 7.31-7.46 (4H, m, C_6H_4)	91
6m	$C_{15}H_{11}ClKN_3OS_2$	11.23 / 10.83	16.77 / 16.53	302-303	—	2.79; 1.78	8.72 (s), 8.19 (d, *J* = 8.7); 7.72 (3H, d, *J* = 8.7, Py)	96
6'f	$C_{21}H_{20}N_4O_2S_2$	13.00 / 13.21	15.46 / 15.09	224-225	13.80	2.80; 1.76	7.40-7.76 (5H, m, C_6H_5), 2.27 (3H, s, CH_3), 3.34 (3H, s, NCH_3)	89
6'g	$C_{17}H_{22}N_8OS_2$	26.34 / 26.77	15.72 / 15.32	242-244	13.56	2.66; 1.76	9.22 (1H, s, NH); 6.82 (1H, s, NH); 6.64 (1H, s, NH); 3.19-3.24 (4H, m); 1.00-1.13 (6H, m, Et_2)	92
7a	$C_{16}H_{13}BrN_2OS_2$	6.85 / 7.12	16.52 / 16.28	229-230	10.60	2.70; 1.74	7.66 (d, *J* = 8.7); 7.56 (4H, d, *J* = 8.7, C_6H_4)	67
7b	$C_{18}H_{17}N_3O_2S_2$	10.98 / 11.32	17.56 / 17.25	238-240	10.44	2.75; 1.72	9.96 (1H, s, NH); 7.60 (d, *J* = 8.8); 7.50 (4H, d, *J* = 8.8, C_6H_4); 2.04 (3H, s, CH_3)	70

TABLE 3. The Characteristics of Compounds **8a-z**,**a'**,**b'**

Com-pound	Empirical formula	Found, % / Calculated, %		mp, °C	^{1}H NMR spectrum, δ, ppm (*J*, Hz)			Yield, %
		N	S		$(CH_2)_4$ (br. d; br. s)	R	R^1	
1	2	3	4	5	6	7	8	9
8a	$C_{21}H_{20}N_2O_2S_2$	6.85 / 7.06	16.38 / 16.17	143-45	2.76 (*J* = 27.8); 1.75	5.95-6.00 (1H, m, CH); 5.83 (d, *J* = 13.0); 5.26 (2H, d, *J* = 16.0, CH_2); 4.86-4.88 (2H, m, CH_2)	7.37-8.10 (5H, m, C_6H_5); 4.62 (2H, s, CH_2)	64
8b	$C_{22}H_{24}N_2O_2S_2$	6.46 / 6.79	15.82 / 15.54	186-187	2.76 (*J* = 26.1); 1.76	7.41-7.59 (5H, m, C_6H_5)	4.26 (2H, s, CH_2); 1.20 (9H, s, *t*-Bu)	74
8c	$C_{24}H_{19}BrN_2O_2S_2$	5.16 / 5.48	12.93 / 12.54	225-226	2.72 (*J* = 28.8); 1.75	7.43-7.60 (5H, m, C_6H_5)	7.94 (d, *J* = 8.7); 7.77 (4H, d, *J* = 8.7, C_6H_4); 4.67 (2H, s, CH_2)	65
8d	$C_{25}H_{20}F_2N_2O_3S_2$	5.36 / 5.62	13.02 / 12.86	209-210	2.73 (*J* = 24.3); 1.75	7.25-7.43 (5H, m C_6H_5)	7.52-7.75 (5H, m, $C_6H_4OCHF_2$-2); 4.53 (2H, s, CH_2)	75
8e	$C_{30}H_{24}N_2O_2S_2$	5.27 / 5.51	12.85 / 12.61	231-232	2.72 (*J* = 32.9); 1.75	7.45-7.55 (5H, m, C_6H_5)	8.10 (d, *J* = 8.4); 7.90 (4H, d, *J* = 8.4, C_6H_4); 7.59-7.79 (5H, m, C_6H_5); 4.75 (2H, s, CH_2)	72
8f	$C_{27}H_{27}N_3O_2S_2$	8.17 / 8.58	13.46 / 13.10	259-260	2..77 (*J* = 12.3); 1.77	7.26-7.38 (5H, m, C_6H_5)	7.42-7.57 (5H, m, C_6H_5); 4.67-4.76 (1H, m, CH); 3.56 (2H, s, CH_2); 1.02 (6H, d, *J* = 6.6, $(CH_3)_2$)	69
8g	$C_{25}H_{22}N_2O_2S_2$	6.04 / 6.27	14.73 / 14.36	213-214	2.72 (*J* = 30.5); 1.75	7.40 (d, *J* = 8.4); 7.30 (4H, d, *J* = 8.1, C_6H_4); 2.42 (3H, s, CH_3)	7.55-8.00 (5H, m, C_6H_5); 4.70 (2H, s, CH_2)	71
8h	$C_{28}H_{29}N_3O_2S_2$	8.07 / 8.34	12.98 / 12.73	246-247	2.77 (*J* = 17.1); 1.78	7.24-7.38 (4H, m, C_6H_4); 2.06 (3H, s, CH_3)	7.40-7.56 (5H, m, C_6H_5); 4.75-4.85 (1H, m, CH); 3.54 (2H, s, CH_2); 1.01 (6H, d, *J* = 6.0, $(CH_3)_2$)	84

TABLE 3 (continued)

1	2	3	4	5	6	7	8	9
8i	$C_{18}H_{18}N_2OS_2$	7.95 / 8.18	18.97 / 18.72	171-172	2.77 (J = 23.9); 1.77	7.30-7.45 (4H, m, C_6H_4); 2.03 (3H, s, CH_3)	2.43 (3H, s, CH_3)	77
8j	$C_{22}H_{15}BrN_4O_5S_2$	9.87 / 10.02	11.87 / 11.46	214-215	2.77 (J = 24.3); 1.78	7.80 (d, J = 8.7); 7.45 (4H, d, J = 8.7, C_6H_4)	8.80 (1H, s); 8.50 (1H, d, J = 8.8); 8.07 (1H, d, J = 8.8, C_6H_3)	78
8k	$C_{24}H_{18}BrClN_2O_2S_2$	4.96 / 5.13	11.92 / 11.75	256-257	2.73 (J = 28.6); 1.75	7.82 (d, J = 8.7); 7.62 (4H, d, J = 8.4, C_6H_4)	8.02 (d, J = 8.7); 7.44 (4H, d, J = 8.7, C_6H_4); 4.70 (2H, s, CH_2)	75
8l	$C_{27}H_{25}Cl_2N_3O_2S_2$	7.31 / 7.52	11.82 / 11.48	226-228	2.74 (br. s); 1.76 (br. t, J = 5.91)	7.97 (1H, s, C_6H_3); 7.67 (2H, s)	7.35-7.96 (5H, m, C_6H_5); 4.75-4.84 (1H, m, CH); 3.60 (2H, q, J = 9.1, CH_2); 1.10 (6H, d, J = 6.5, $(CH_3)_2$)	71
8m	$C_{25}H_{21}BrN_2O_3S_2$	5.02 / 5.17	12.0 / 11.84	215-216	2.70 (J = 26.4); 1.73	7.14-7.57 (4H, m, C_6H_4); 3.80 (3H, s, OCH_3)	7.94 (d, J = 8.7); 7.78 (4H, d, J = 8.7, C_6H_4); 4.68 (2H, q, J = 28.6, CH_2)	74
8n	$C_{29}H_{30}N_2O_3S_2$	5.27 / 5.40	12.64 / 12.36	189-190	2.72 (J = 32.1); 1.75	3.85 (3H, s, OCH_3); 7.34 (d, J = 8.7); 7.13 (4H, d, J = 8.7, C_6H_4)	7.90 (d, J = 8.7); 7.60 (4H, d, J = 8.7, C_6H_4); 4.70 (2H, s, CH_2); 1.32 (9H, s, $(CH_3)_3$)	69
8o	$C_{25}H_{21}ClN_2O_3S_2$	5.25 / 5.64	13.15 / 12.90	233-234	2.73 (J = 32.1); 1.75	7.30 (d, J = 8.7); 7.10 (4H, d, J = 8.7, C_6H_4); 3.85 (3H, s, OCH_3)	8.00 (d, J = 8.4); 7.61 (4H, d, J = 8.4, C_6H_4); 4.64 (2H, s, CH_2)	78
8p	$C_{25}H_{19}F_3N_2O_3S_2$	5.18 / 5.42	12.80 / 12.41	234-236	2.73 (J = 28.6); 1.75	7.35-7.50 (5H, m, C_6H_4–$OCHF_2$-4)	7.51-8.11 (4H, m, C_6H_4); 4.70 (2H, s, CH_2)	79
8q	$C_{25}H_{19}ClF_2N_2O_3S_2$	5.02 / 5.26	12.47 / 12.03	243-244	2.73 (J = 28.30); 1.75	7.50 (d; J = 9.0); 7.40 (5H, d, J = 8.7, C_6H_4–$OCHF_2$-4)	8.03 (d, J = 8.7); 7.66 (4H, d, J = 8.7, C_6H_4); 4.70 (2H, s, CH_2)	80
8r	$C_{26}H_{21}ClF_2N_2O_3S_2$	4.96 / 5.12	11.95 / 11.72	188-189	2.73 (J = 26.4); 1.75	7.20-7.50 (5H, m, C_6H_4–$OCHF_2$-4)	8.10 (d, J = 8.7); 7.60 (4H, d, J = 8.7, C_6H_4); 5.50 (1H, q, J = 23.3, CH); 1.4 (3H, d, J = 7.2, CH_3)	78
8s	$C_{26}H_{20}F_4N_2O_4S_2$	4.64 / 4.96	11.75 / 11.36	211-213	2.74 (J = 29.9); 1.74	7.20-7.70 (5H, m, C_6H_4–$OCHF_2$-4)	7.20-8.10 (5H, m, $C_6H_4OCHF_2$-4); 4.70 (2H, s, CH_2)	81
8t	$C_{27}H_{22}F_2N_2O_5S_2$	5.24 / 5.03	11.81 / 11.52	212-214	2.75 (J = 26.2); 1.76	7.20-7.60 (5H, m, C_6H_4–$OCHF_2$-4)	7.00-7.50 (3H, m, C_6H_3); 4.65 (2H, s, CH_2); 4.31 (4H, q, J = 11.8, $(OCH_2)_2$)	82

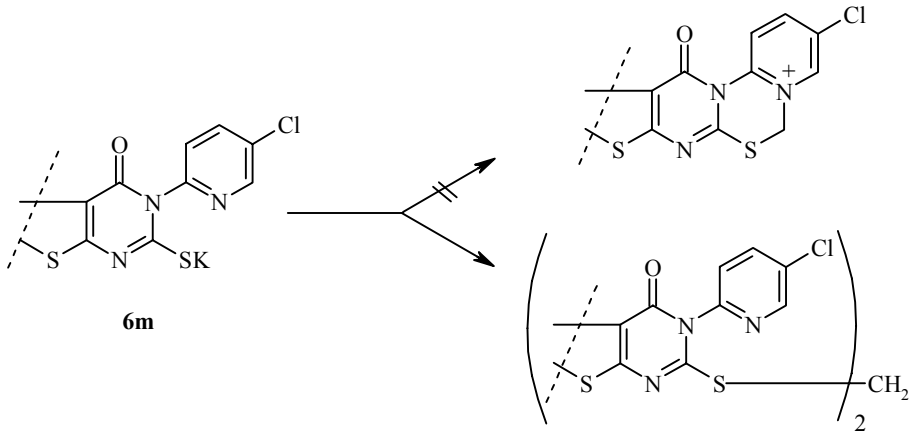
TABLE 3 (continued)

1	2	3	4	5	6	7	8	9
8u	$C_{25}H_{21}ClN_2O_2S_2$	5.43 / 5.82	13.77 / 13.33	190-191	2.73 (br. d, J = 49.5); 1.75 (br. d, J = 4.9)	7.25-7.34 (5H, m, C_6H_5); 5.33 (2H, s, CH_2)	8.03 (4H, d, J = 8.7, C_6H_4); 7.66 (d, J = 8.7); 4.79 (2H, s, CH_2)	81
8v	$C_{28}H_{29}N_3O_2S_2$	8.06 / 8.34	12.95 / 12.73	202-203	2.77 (J = 33.9); 1.75	7.20-7.35 (5H, m, C_6H_5); 5.25 (2H, s, CH_2)	7.36-7.55 (5H, m, C_6H_5); 4.77 (1H, s, CH); 3.64 (2H, s, CH_2); 1.01 (6H, d, J = 6.6, $(CH_3)_2$)	84
8w	$C_{24}H_{19}N_5O_6S_2$	12.87 / 13.03	12.18 / 11.92	230-231	2.77 (J = 26.0); 1.76	10.22 (1H, s, NH); 7.73 (d, J = 8.8); 7.42 (4H, d, J = 8.8, C_6H_4); 2.20 (3H, s, CH_3)	8.80 (s); 8.47 (d, J = 8.8); 8.10 (3H, d, J = 8.8, C_6H_3)	83
8x	$C_{26}H_{22}FN_3O_3S_2$	8.00 / 8.28	12.93 / 12.62	272	2.71 (J = 30.3); 1.74	10.22 (1H, s, NH); 7.75 (d, J = 8.7); 7.34 (4H, d, J = 8.7, C_6H_4); 2.20 (3H, s, CH_3)	7.30-8.10 (4H, m, C_6H_4); 4.68 (2H, s, CH_2)	85
8y	$C_{29}H_{30}N_4O_3S_2$	9.84 / 10.26	11.98 / 11.72	173-174	2.63 (br. s); 1.77 (br. s)	10.20 (1H, s, NH); 7.70 (d, J = 8.7); 7.30 (4H, d, J = 8.5, C_6H_4); 2.10 (3H, s, CH_3)	7.30-7.50 (5H, m, C_6H_5); 4.79 (1H, s, CH); 3.56 (2H, s, CH_2); 1.02 (6H, d, J = 7.7, $(CH_3)_2$)	83
8z	$C_{28}H_{27}FN_4O_2S_2$	10.05 / 10.49	12.27 / 11.98	193-194	2.75 (J = 29.1); 1.76	9.20 (1H, s, CH); 7.35-7.42 (4H, m, C_6H_4)	7.40-8.00 (5H, m, C_6H_5); 4.82 (1H, s, CH); 3.56 (2H, s, CH_2); 1.01 (6H, d, J = 9.9, $(CH_3)_2$)	81
8'a	$C_{26}H_{25}ClN_4O_2S_2$	10.31 / 10.67	12.59 / 12.21	185-186	2.76 (J = 13.2); 1.79	8.78 (s); 8,27 (d, J = 8.7); 7.72 (3H, d, J = 8.7, 5-Cl–Py)	7.35-7.54 (5H, m, C_6H_5); 4.78 (1H, s, CH); 3.58 (2H, s, CH_2); 1.01 (6H, d, J = 6.6, $(CH_3)_2$)	85
8'b	$C_{27}H_{22}N_6O_6S_2$	14.02 / 14.23	11.06 / 10.86	225	2.80 (J = 27.0); 1.76	7.40-7.76 (5H, m, C_6H_5), 3.34 (3H, s, NCH_3), 2.27 (3H, s, CH_3)	8.86 (s); 8.50 (d, J = 8.8); 8.14 (3H, d, J = 8.8, C_6H_3)	82

reaction of compound **2b** with *p-tert*-butyl-α-bromoacetophenone led to the formation of the thiazoline derivative – 3-ethoxycarbonyl-2-[4-(*p-tert*-butylphenyl)-3-phenyl-2-thiazolinylideneamino]-4,5,6,7-tetrahydrobenzo[*b*]thiophene picrate (**9**).

Di[3-(5-chloro-2-pyridyl)-4-oxo-3H-5,6,7,8-tetrahydrobenzo[*b*]thieno[2,3-*d*]pyrimidin-2-ylthio]methane was isolated in the reaction of compound **6m** with methylene chloride (Scheme 3).

Scheme 3



6m **10**

The structure of the synthesized compounds was confirmed by data from elemental analysis and ^{1}H NMR spectra (Tables 1-3).

EXPERIMENTAL

The ^{1}H NMR spectra of the synthesized compounds were recorded on a Bruker-300 instrument (300 MHz) with DMS0-d_6 as solvent and TMS as internal standard.

The initial 2-amino-3-ethoxycarbonyl-4,5,6,7-tetrahydrobenzo[*b*]thiophene (**1**) and 3-ethoxycarbonyl-2-isothiocyanato-4,5,6,7-tetrahydrobenzo[*b*]thiophene (**3**) respectively were synthesized by the methods described in [6, 9].

3-Ethoxycarbonyl-2-N-R-thioureido-4,5,6,7-tetrahydrobenzo[*b*]thiophenes (2a-r, 4). A. To a solution of 2-amino-3-ethoxycarbonyl-4,5,6,7-tetrahydrobenzo[*b*]thiophene (2.25 g, 10 mmol) in ethanol (20 ml) we added the respective isothiocyanate (10 mmol). The reaction mixture was boiled for 3-4 h and cooled, and the precipitate was filtered off. Compounds **2a-c**,**g**,**i**,**j** were obtained

B. To a solution of the respective amine in ethanol (30 ml) we added 3-ethoxycarbonyl-2-isothiocyanato-4,5,6,7-tetrahydrobenzo[*b*]thiophene (2.67 g, 10 mmol). The reaction mixture was boiled for 4-6 h and cooled, and the precipitate was filtered off. Compounds **2b-r** and **4** were obtained.

2-(2-Aminobenzothiazolyl)-3-ethoxycarbonyl-4,5,6,7-tetrahydrobenzo[*b*]thiophene (5). This compound was obtained from 3-ethoxycarbonyl-2-isothiocyanato-4,5,6,7-tetrahydrobenzo[*b*]thiophene and *o*-aminothiophenol by method B.

Potassium Salts of 3-R-2-Mercapto-3,4,5,6,7,8-hexahydrobenzo[*b*]thieno[2,3-*d*]pyrimidin-4-ones (6a,c-f,h,k,m). A solution of the respective 2-(N-R-thioureido)-3-ethoxycarbonyl-4,5,6,7-tetrahydrobenzo-[*b*]thiophene (10 mmol) and potassium hydroxide (1.12 g, 20 mmol) in ethanol (20 ml) was boiled for 3-4 h and cooled, and the precipitate was filtered off.

3-R-2-Thioxo-1,2,3,4,5,6,7,8-octahydrobenzo[*b*]thieno[2,3-*d*]pyrimidin-4-ones (6'a-g). A solution of the respective 3-ethoxycarbonyl-2-(N-R-thioureido)-4,5,6,7-tetrahydrobenzo[*b*]thiophene (10 mmol) and potassium hydroxide (1.12 g, 20 mmol) in ethanol (20 ml) was boiled for 3-4 h. The reaction mixture was poured into water, neutralized with glacial acetic acid, and cooled. The precipitate was filtered off.

2-R-Amino-4(H)-5,6,7,8-tetrahydrobenzo[*b*]thieno[2,3-*d*]-1,3-thiazin-4-ones (7a, b). Compound **2e**,**k** (10 mmol) was dissolved in concentrated sulfuric acid (15 ml), and the solution was left at 18-20°C for 24 h. It was then poured into iced water (100 ml) and neutralized with ammonia. The precipitate was filtered off.

The Picrate of 3-Ethoxycarbonyl-2-[4-(*p-tert*-butyl)-3-phenyl-2-thiazolinylideneamino]-4,5,6,7-tetrahydrobenzo[*b*]thiophene (9). Compound **2b** (3.6 g, 10 mmol) and *p-tert*-butyl-α-bromoacetophenone (2.53 g, 10 mmol) were boiled in ethanol (25 ml) for 4 h and cooled. A saturated solution of picric acid was added, and the precipitate was filtered off.

S-Substituted 3-R-2-Mercapto-3,4,5,6,7,8-hexahydrobenzo[*b*]thieno[2,3-*d*]pyrimidin-4-ones (8a',b'). To a solution of the potassium salt **6** (10 mmol) in ethanol (20-30 ml) [ready prepared or obtained by dissolving compound **6'** (10 mmol) in an alcohol solution (20-30 ml) of potassium hydroxide (0.056 g, 10 mmol)] we added the alkylating agent (10 mmol). The reaction mixture was left at 20°C for 20-24 h, and the precipitate was filtered off.

Di[3-(5-chloro-2-pyridyl)-4-oxo-3H-5,6,7,8-tetrahydrobenzo[*b*]thieno[2,3-*d*]pyrimidin-2-ylthio]-methane (10). To a solution of methylene chloride (0.85 g, 10 mmol) in ethanol (10 ml) we added dropwise with stirring a solution of the potassium salt **6m** (10 mmol) in aqueous ethanol (20 ml). The mixture was left at 20°C for 24 h and was then boiled for 1 h and cooled. The precipitate was filtered off. Yield 52%; mp 295-296°C (from DMF). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.68-1.82 [8H, m, 2 $(CH_2)_4$]; 2.65-2.83 [8H, m, 2 $(CH_2)_4$]; 4.90 (2H, s, CH_2); 7.72 (2H, d, *J* = 8.7, H_{Py}); 8.70 [2H, s, 6-H $(5\text{-Cl-Py})_2$]. Found %: N 12.0; S 18.46. $C_{31}H_{24}Cl_2N_6O_2S_4$. Calculated %: N 11.81; S 18.00.

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