Synthesis and cyclization of 3-substituted 1-(3-cyano-4,5,6,7-tetrahydrobenzo[*b*]thien-2-yl)thioureas

P. PAZDERA, M. ŘEZKA, and E. NOVÁČEK

Department of Organic Chemistry, Faculty of Natural Sciences, J. E. Purkyně University, CS-611 37 Brno

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New 3-substituted 1-(3-cyano-4,5,6,7-tetrahydrobenzo[*b*]thien-2-yl)-thioureas were prepared by the reaction of 2-isothiocyanato-3-cyano-4,5,6,7-tetrahydrobenzo[*b*]thiophene with primary amines (ethyl-, isopropyl-, *tert*-butyl-, cyclohexylamine, aniline, 4-nitroaniline, 4-anisidine, phenylhydrazine, 4-hydrazinobenzonitrile, ethyl 4-hydrazinobenzoate, hydrazine) in the mixture of dichloromethane and petroleum ether. Besides 3-amino-1-(3-cyano-4,5,6,7-tetrahydrobenzo[*b*]thien-2-yl)thiourea, 3-amino-4-imino-5,6,7,8-tetrahydrobenzo[*b*]thieno[2,3-*d*]-1,2,3,4-tetrahydropyrimidine-2-thione as a product of cyclization was formed.

3-Substituted 1-(3-cyano-4,5,6,7-tetrahydrobenzo[*b*]thien-2-yl)thioureas underwent in boiling ethylene glycol monomethyl ether the cyclization to 3-substituted 4-imino-5,6,7,8-tetrahydrobenzo[*b*]thieno[2,3-*d*]-1,2,3,4-tetrahydropyrimidine-2-thiones. 3-Isopropyl, 3-*tert*-butyl, and 3-cyclohexyl derivatives did not react.

Были синтезированы новые 3-замещенные 1-(3-циано-4,5,6,7-тетрагидробензо[*b*]тиен-2-ил)тиомочевины посредством реакции 2-изотиоцианато-3-циано-4,5,6,7-тетрагидробензо[*b*]тиофена с первичными аминами (этил-, изопропил-, *трет*-бутил-, циклогексиламином, анилином, 4-нитроанилином, 4-анизидином, фенилгидразином, 4-гидразинобензонитрилом, этил-4-гидразинобензоатом, гидразином) в смеси дихлорметана с петролейным эфиром. 3-Амино-1-(3-циано-4,5,6,7-тетрагидробензо[*b*]тиен-2-ил)тиомочевина образовывалась наряду с продуктом циклизации, т.е. 3-амино-4-имино-5,6,7,8-тетрагидробензо[*b*]тиено[2,3-*d*]-1,2,3,4-тетрагидропиримидин-2-тионом.

3-Замещенные 1-(3-циано-4,5,6,7-тетрагидробензо[*b*]тиен-2-ил)тиомочевины были подвергнуты циклизации путем варки в монометиловом эфире этиленгликоля, что вело к образованию соответствующих 3-замещенных 4-имино-5,6,7,8-тетрагидробензо[*b*]тиено[2,3-*d*]-1,2,3,4-тетрагидропиримидин-2-тионов. 3-Изопропил, 3-*трет*-бутил-, а также 3-циклогексил-производные не реагировали подобным образом.

Aromatic or heterocyclic 2-aminonitriles are known to form in the reaction with thiourea condensed 4-amino-1,2-dihydropyrimidine-2-thiones. They react

with aryl isothiocyanates under formation of condensed 3-substituted 4-imino--1,2,3,4-tetrahydropyrimidine-2-thiones [1]. One can assume that the intermediate of the reaction might be the corresponding 2-cyano derivative of thiourea. Under the conditions of the reaction this cyclizes — it means that the nitrogen atom of the thioureido group enters into intramolecular interaction with the cyano group.

Authors of paper [2] succeeded in isolating 3-phenyl-1-(2-cyanophenyl)-thiourea after reaction of 2-aminobenzonitrile with phenyl isothiocyanate at 50 °C without any solvent. The reaction was unsuccessfully reproduced [3]; the product of the reaction was always the product of cyclization, *i.e.* 3-phenyl-4--imino-1,2,3,4-tetrahydroquinoline-2-thione even under broadly varied reaction conditions. But the uncyclic compound was successfully prepared by the addition of aniline to 2-isothiocyanatobenzonitrile in the medium with a low polarity (in the mixture of dichloromethane and petroleum ether).

In [4] the reaction of 2-isothiocyanatobenzonitrile with primary amines was studied. In dependence on the reaction conditions (temperature, solvent) either 3-substituted 1-(2-cyanophenyl)thioureas or 3-substituted 4-imino-1,2,3,4--tetrahydroquinazoline-2-thiones and their mixtures were formed. 3-Substituted 1-(2-cyanophenyl)thioureas cyclized in boiling ethanol. The rate of the reaction is the function of both the basicity of the nitrogen atom attacking the cyano group and the branching of the substituent being at that atom. The steric hindrance was the reason why 3-*tert*-butyl-1-(2-cyanophenyl)thiourea did not react.

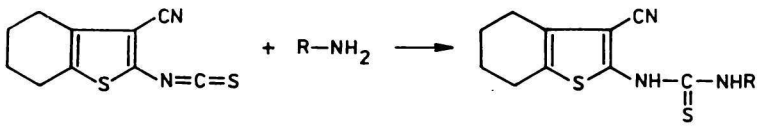
The aim of this work was the preparation of 3-substituted 1-(3-cyano-4,5,6,7--tetrahydrobenzo[*b*]thien-2-yl)thioureas by the reaction of 2-isothiocyanato-3--cyano-4,5,6,7-tetrahydrobenzo[*b*]thiophene with amines (Scheme 1) and their cyclization to 3-substituted 4-imino-5,6,7,8-tetrahydrobenzo[*b*]thieno[2,3-*d*]--1,2,3,4-tetrahydropyrimidine-2-thiones.

Experimental

Melting points were measured on a Kofler hot stage Rapido 79-2106 (Wägetechnik). Elemental analyses were carried out on C. Erba analyzer, Model 1102.

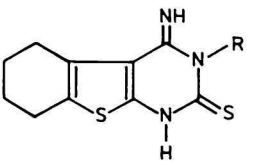
The course of the reactions and the purity of synthesized compounds were checked by TLC on Silufol UV 254 (Kavalier, Votice), chromatograms were detected with instrument Fluotest Universal (Quarzlampen, Hanau). Chromatograms were eluted with benzene, chloroform, diisopropyl ether, diethyl ether and acetonitrile in a container saturated with the vapours of the used solvent.

IR spectra were taken on spectrometer Unicam SP 1000 in KBr pellets, ^{1}H NMR spectra on Tesla BS 567 (100 MHz) instrument in hexadeuteroacetone (internal standard



I–XI

		R
I,	*XII*	C_2H_5
II		$(CH_3)_2CH$
III		$(CH_3)_3C$
IV		cyclo C_6H_{11}
V,	*XIII*	C_6H_5
VI,	*XIV*	$4\text{-}NO_2C_6H_4$
VII,	*XV*	$4\text{-}CH_3OC_6H_4$
VIII,	*XVI*	C_6H_5NH
IX,	*XVII*	$4\text{-}CNC_6H_4NH$
X,	*XVIII*	$4\text{-}C_2H_5OCOC_6H_4NH$
XI,	*XIX*	NH_2



XII–XIX

Scheme 1

TMS) or in hexadeuterodimethyl sulfoxide (internal standard HMDSO); $c = 1$ mol dm^{-3} or saturated solution of the compound.

Characteristics of the synthesized compounds are presented in Tables 1—6.

3-Substituted 1-(3-cyano-4,5,6,7-tetrahydrobenzo[b]thien-2-yl)thioureas I—X

The solution of amine (25 mmol) in dichloromethane (10—50 cm^3) was at room temperature dropwise added into solution of 2-isothiocyanato-3-cyano-4,5,6,7-tetrahydrobenzo[*b*]thiophene [5] (5.5 g; 25 mmol) in the mixture (75 cm^3) of dichloromethane and petroleum ether ($\varphi_r = 1:1$). The reaction mixture was stirred until the starting thiophene derivative was present (checked by TLC). Then the product was filtered off, washed with dichloromethane and dried in vacuum at room temperature. Yellow or yellowish brown crystals were formed.

3-Substituted 4-imino-5,6,7,8-tetrahydrobenzo[b]thieno[2,3-d]-pyrimidine-2-thiones XII—XVIII

Suspension of compound *I* or *V—X* (5 mmol) in ethylene glycol monomethyl ether (25 cm^3) was heated to reflux for 60—240 min. When the starting compound disappeared

Table 1

Characteristics of synthesized 3-substituted 1-(3-cyano-4,5,6,7-tetrahydrobenzo[*b*]thien-2-yl)thioureas and their reaction times

Compound	Formula	M_r	w_i(calc.)/% w_i(found)/%			Yield %	M.p. °C	R_f (Diethyl ether)	τ/min
			C	H	N				
I	$C_{12}H_{15}N_3S_2$	265.39	54.31	5.67	15.83	85	185—187	0.62	20
			54.25	5.60	15.74				
II	$C_{13}H_{17}N_3S_2$	279.42	55.88	6.13	15.04	86	201—203	0.66	20
			55.80	6.00	14.97				
III	$C_{14}H_{19}N_3S_2$	293.44	57.30	6.59	14.32	96	186—188	0.72	20
			57.30	6.45	14.28				
IV	$C_{16}H_{21}N_3S_2$	319.48	60.15	6.63	13.15	88	209—211	0.82	20
			60.10	6.55	13.08				
V	$C_{16}H_{15}N_3S_2$	313.44	61.31	4.82	13.41	95	171—173	0.69	60
			61.25	4.75	13.35				
VI	$C_{16}H_{14}N_4O_2S_2$	359.45	53.46	3.93	15.59	81	202—204	0.15	180
			53.50	3.86	15.60				
VII	$C_{17}H_{17}N_3OS_2$	343.46	59.45	4.99	12.23	95	165—167	0.58	45
			59.40	4.90	12.20				
VIII	$C_{16}H_{16}N_4S_2$	328.45	58.51	4.91	17.06	87	154—156	0.61	30
			58.45	4.85	17.00				
IX	$C_{17}H_{15}N_5S_2$	353.46	57.77	4.27	19.81	85	180—181	0.35	60
			57.70	4.12	19.75				
X	$C_{19}H_{20}N_4O_2S_2$	400.51	56.98	5.03	13.99	82	185—187	0.33	40
			56.89	4.95	13.94				

Table 2

IR spectral characteristics of synthesized compounds *I*—*X*

Compound	$\tilde{\nu}$/cm^{-1}					
	ν(C≡N)	ν(NHCS)	ν(NH)	ν(C=C)	ν(C_{sp^3}H)	
I	2210	1540, 1250	3220, 3280	1580	2950, 2890	
II	2210	1535, 1240	3210, 3280	1580	2950, 2920, 2880	
III	2210	1555, 1225	3180, 3310	1590	2950, 2920, 2890	
IV	2210	1530, 1250	3210, 3280	1570	2970, 2930, 2880	
V	2210	1555, 1230	3200, 3290	1605, 1580	2950, 2880	
VI	2210	1540, 1250	3200, 3300	1600, 1580	2960, 2890	1350, 1520[a]
VII	2210	1560, 1240	3210, 3300	1590, 1570	2940, 2980	1040[b]
VIII	2210	1555, 1230	3200, 3240, 3310	1580	2950, 2880	
IX	2200, 2300	1550, 1260	3190, 3280, 3300	1570	2950, 2890	
X	2210	1550, 1270	3170, 3220, 3300	1600, 1580	2950, 2870	1715[c], 1180[d]

a) $\nu_{s,as}(NO_2)$; *b*) ν(COC); *c*) ν(C=O); *d*) ν(COC).

Table 3

^{1}H NMR spectral characteristics of synthesized compounds *I*—*X*

Compound	δ/ppm
I[a]	8.25 (s, 1H, NH), 9.20 (s, 1H, NH), 1.58—1.90 (m, 4H, CH_2), 2.34—2.80 (m, 4H, CH_2), 3.58 (q, 2H, CH_2, J = 6.5 Hz), 1.12 (t, 3H, CH_3, J = 6.5 Hz)
II[b]	7.89 (s, 1H, NH), 9.35 (s, 1H, NH), 1.60—1.82 (m, 4H, CH_2), 2.38—2.60 (m, 4H, CH_2), 4.33 (m, 1H, CH, J = 6.0 Hz), 1.12 (d, 6H, CH_3, J = 6.0 Hz)
III[a]	8.55 (s, 2H, NH), 1.62—1.90 (m, 4H, CH_2), 2.38—2.66 (m, 4H, CH_2), 1.43 (s, 9H, CH_3)
IV[a]	8.68 (s, 2H, NH), 1.00—2.72 (m, 19H, CH + CH_2)
V[b]	9.60 (s, 1H, NH), 9.72 (s, 1H, NH), 1.65—1.93 (m, 4H, CH_2), 2.49—2.80 (m, 4H, CH_2), 7.12—7.60 (m, 5H, H_{arom})
VI[a]	11.00 (s, 2H, NH), 1.62—1.92 (m, 4H, CH_2), 2.40—2.76 (m, 4H, CH_2), 8.00—8.40 (m, 4H, H_{arom})
VII[b]	10.52 (s, 1H, NH), 9.82 (s, 1H, NH), 1.65—1.89 (m, 4H, CH_2), 2.42—2.80 (m, 4H, CH_2), 7.20—7.72 (m, 4H, H_{arom}), 3.83 (s, 3H, OCH_3)
VIII[a]	9.61 (s, 1H, NH), 9.87 (s, 1H, NH), 10.23 (s, 1H, NH), 1.64—1.93 (m, 4H, CH_2), 2.45—2.82 (m, 4H, CH_2), 7.14—7.48 (m, 5H, H_{arom})
IX[b]	8.42 (s, 1H, NH), 9.70 (s, 1H, NH), 10.25 (s, 1H, NH), 1.75—1.90 (m, 4H, CH_2), 2.50—2.75 (m, 4H, CH_2), 7.10—7.85 (m, 4H, H_{arom})
X[a]	8.92 (s, 1H, NH), 10.38 (s, 1H, NH), 10.52 (s, 1H, NH), 1.62—1.93 (m, 4H, CH_2), 2.42—2.75 (m, 4H, CH_2), 7.75—8.10 (m, 2H, H_{arom}), 6.75—7.00 (m, 2H, H_{arom}), 4.30 (q, 2H, CH_2, J = 8.0 Hz), 1.33 (t, 3H, CH_3, J = 8.0 Hz)

Spectra measured in solution *a*) of hexadeuterodimethyl sulfoxide — internal standard HMDSO or *b*) of hexadeuteroacetone — internal standard TMS.

the solvent was evaporated on a rotating evaporator and the rest crystallized from ethanol with charcoal giving a beige crystalline compound.

3-Amino-4-imino-5,6,7,8-tetrahydrobenzo[b]thieno[2,3-d]-1,2,3,4--tetrahydropyrimidine-2-thione (XIX)

Solution of hydrazine hydrate (0.8 g of 100 %; 25 mmol) in dichloromethane (50 cm^3) was dropwise added into solution of 2-isothiocyanato-3-cyano-4,5,6,7-tetrahydrobenzo[*b*]thiophene (5.5 g; 25 mmol) in the mixture (75 cm^3) of dichloromethane—petroleum ether ($\varphi_r = 1:1$). After 20 min petroleum ether (50 cm^3) was added and the crystals were filtered off. The mixture of *XI* and *XIX* so formed was suspended in ethanol (100 cm^3) and refluxed for 2 h. Then the mixture was cooled down to room temperature, the crystals of compound *XIX* were filtered off, washed with ethanol and dried in a vacuum oven at room temperature giving a beige crystalline compound.

Results and discussion

The first step of our work was aimed at the addition of primary amines to 2-isothiocyanato-3-cyano-4,5,6,7-tetrahydrobenzo[*b*]thiophene in order to isolate 3-substituted 1-(3-cyano-4,5,6,7-tetrahydrobenzo[*b*]thien-2-yl)thioureas *I*—*XI* (Scheme 1). We knew that these compounds could enter the cyclization reaction to 3-substituted 4-imino-5,6,7,8-tetrahydrobenzo[*b*]thieno[2,3-*d*]--1,2,3,4-tetrahydropyrimidine-2-thiones *XII*—*XIX* similarly as it was observed during the synthesis of 3-substituted 1-(2-cyanophenyl)thioureas by the addition of amines to 2-isothiocyanatobenzonitrile [3, 4].

So we tried to carry out the reaction under such conditions as to suppress the cyclization and to be able to isolate the expected compounds directly from the reaction mixture in a pure crystalline form. During the crystallization they could again cyclize. That was the reason why we carried out the reactions of 2-isothiocyanato-3-cyano-4,5,6,7-tetrahydrobenzo[*b*]thiophene with ethylamine in the medium of very low polarity (dichloromethane and petroleum ether) at the temperature of 0 °C. During the addition of dichloromethane solution of ethylamine the product — 3-ethyl-1-(3-cyano-4,5,6,7-tetrahydrobenzo[*b*]thien-2--yl)thiourea (*I*) precipitated. TLC proved that compound *I* is the only product formed. The same results were achieved at room temperature but the reaction time was shortened to one third.

The structure of compound *I* was confirmed by IR and ^{1}H NMR spectroscopies. In the IR spectrum the stretching vibration of the cyano group at $\tilde{\nu} = 2210\ cm^{-1}$, the bands of thioureido group vibration at $\tilde{\nu} = 1250$ and $1540\ cm^{-1}$ and the bands of vibrations of both amino groups at $\tilde{\nu} = 3220$ and

Table 4

Characteristics of 3-substituted 4-imino-5,6,7,8-tetrahydrobenzo[*b*]thieno[2,3-*d*]-1,2,3,4-tetrahydropyrimidine-2-thiones *XII*—*XIX* and their reaction times

Compound	Formula	M_r	w_i(calc.)/% / w_i(found)/%			Yield / %	M.p. / °C	τ/min
			C	H	N			
XII	$C_{12}H_{15}N_3S_2$	265.39	54.31 54.21	5.67 5.60	15.83 15.70	78	214—216	40
XIII	$C_{16}H_{15}N_3S_2$	313.44	61.31 61.25	4.82 4.78	13.41 13.33	85	205—206	90
XIV	$C_{16}H_{14}N_4O_2S_2$	359.45	53.46 53.60	3.93 3.94	15.59 15.59	75	329—332	180
XV	$C_{17}H_{17}N_3OS_2$	343.46	59.45 59.41	4.99 4.90	12.23 12.18	90	220—222	60
XVI	$C_{16}H_{16}N_4S_2$	328.45	58.51 58.45	4.91 4.80	17.06 16.99	96	234—236	60
XVII	$C_{17}H_{15}N_5S_2$	353.46	57.77 57.70	4.27 4.19	19.81 19.78	82	270—271	90
XVIII	$C_{19}H_{20}N_4O_2S_2$	400.51	56.98 56.90	5.03 4.90	13.99 14.00	88	236—238	80
XIX	$C_{10}H_{12}N_4S_2$	252.35	47.60 47.50	4.79 4.70	22.20 22.10	85	299—303	

Table 5

IR spectral characteristics of synthesized compounds *XII*—*XIX*

Compound	$\tilde{\nu}$/cm^{-1}					
	ν(C═N)	ν(NHCS)	ν(NH)	ν(C═C)	ν(C_{sp^3}H)	
XII	1650	1520, 1260	3150, 3270	1570	2980, 2880, 2940	
XIII	1630	1540, 1260	3150, 3240	1580, 1490	2920, 2880	
XIV	1630	1520, 1250	3200, 3300	1580, 1600	2940, 2860	1535, 1340[a]
XV	1610	1530, 1240	3300, 3400	1580, 1600	2950, 2870	1030[b]
XVI	1640	1540, 1230	3230, 3250, 3290	1580, 1600	2940, 2840	
XVII	1630	1540, 1250	3210, 3240, 3380	1570, 1600	2940, 2850	2240[c]
XVIII	1620	1560, 1270	3220, 3280, 3400	1590, 1600	2950, 2870	1710[d] 1190[e]
XIX	1630	1540, 1260	3120, 3170, 3250, 3340	1570	2950, 2860	

a) $\nu_{s,as}(NO_2)$; *b*) ν(COC); *c*) ν(C≡N); *d*) ν(C═O); *e*) ν(COC).

Table 6

^{1}H NMR spectral characteristics of synthesized compounds *XII*—*XIX*

Compound	δ/ppm
XII[a]	1.81—2.00 (m, 4H, CH_2), 2.54—3.00 (m, 4H, CH_2), 4.75 (q, 2H, CH_2, J = 6.5 Hz), 1.25 (t, 3H, CH_3, J = 6.5 Hz)
XIII[a]	1.75—2.00 (m, 4H, CH_2), 2.60—3.20 (m, 4H, CH_2), 7.08—7.80 (m, 5H, H_{arom})
XIV[a]	1.63—2.00 (m, 4H, CH_2), 2.60—3.20 (m, 4H, CH_2), 7.75—8.48 (m, 4H, H_{arom})
XV[a]	1.62—2.00 (m, 4H, CH_2), 2.60—2.82 (m, 2H, CH_2), 2.87—3.20 (m, 2H, CH_2), 3.85 (s, 3H, CH_3), 6.85—7.75 (m, 4H, H_{arom})
XVI[a]	1.63—2.00 (m, 4H, CH_2), 2.60—2.75 (m, 2H, CH_2), 2.80—3.04 (m, 2H, CH_2), 6.50—7.20 (m, 5H, H_{arom})
XVII[a]	9.00 (s, 3H, NH), 1.63—2.00 (m, 4H, CH_2), 2.50—3.00 (m, 4H, CH_2), 6.72—7.80 (m, 4H, H_{arom})
XVIII[a]	9.82 (s, 2H, NH), 11.28 (s, 1H, NH), 1.65—2.00 (m, 4H, CH_2), 2.60—2.75 (m, 2H, CH_2), 2.79—3.00 (m, 2H, CH_2), 6.92—8.00 (m, 4H, H_{arom}), 1.32 (t, 3H, CH_3, J = 8.0 Hz), 4.60 (q, 2H, CH_2, J = 8.0 Hz)
XIX[b]	1.90—2.13 (m, 4H, CH_2), 2.75—3.08 (m, 4H, CH_2)

Spectra measured in *a*) hexadeuterodimethyl sulfoxide (internal standard HMDSO), c = 1 mol dm^{-3} or saturated solution of the compound or in *b*) saturated solution in trifluoroacetic acid.

3280 cm^{-1} were observed. In the ^1H NMR spectrum signals of protons at N-1 atom at $\delta = 9.20$ ppm, at N-3 at $\delta = 8.25$ ppm and ethyl group as well as methylene groups of condensed cyclohexane ring appeared (Table 3).

These results led us to the repeated reactions of 2-isothiocyanato-3-cyano--4,5,6,7-tetrahydrobenzo[*b*]thiophene with the other amino derivatives mentioned in Scheme 1.

In all cases 3-substituted 1-(3-cyano-4,5,6,7-tetrahydrobenzo[*b*]thien-2--yl)thioureas *II*—*X* were formed in the yields of 81—90 %. Their reaction times, yields, melting points, and R_f values are presented in Table 1. The structure of *II*—*X* was confirmed using the IR and ^1H NMR spectroscopic data (Tables 2 and 3) analogously to the spectra of compound *I* discussed above.

The only exception was the addition of hydrazine hydrate to 2-isothiocyanato-3-cyano-4,5,6,7-tetrahydrobenzo[*b*]thiophene when even at room temperature both 3-amino-1-(3-cyano-4,5,6,7-tetrahydrobenzo[*b*]thien-2-yl)thiourea (*XI*) and the product of its cyclization, 3-amino-4-imino-5,6,7,8-tetrahydrobenzo[*b*]thieno[2,3-*d*]-1,2,3,4-tetrahydropyrimidine-2-thione (*XIX*), were formed. This was proved on the one hand by TLC of the product isolated after reaction and on the other hand by the analysis of IR spectrum. Compound *XI* is characterized with bands at $\tilde{\nu} = 2210\ cm^{-1}$ (stretch in cyano group), at $\tilde{\nu} = 3140$, 3240, 3320 cm^{-1} (stretch in N—H) and at $\tilde{\nu} = 1260$ and 1560 cm^{-1} (stretch in thioureido group). The spectral characteristics are given in Tables 5 and 6.

The result of the addition of hydrazine hydrate at 0 °C was similar. The mixture of *XI* and *XIX* formed could be united to pure compound *XIX* in boiling ethanol.

The subsequent part of our work was concentrated on the cyclization of 3-substituted 1-(3-cyano-4,5,6,7-tetrahydrobenzo[*b*]thien-2-yl)thioureas *I*—*X*. At first the cyclization was carried out in boiling ethanol and the progress of the reaction was followed by TLC. It was proved that only compound *I* cyclized (fully after 15 h of reaction). The other compounds did not cyclize. It was rather surprising because the time of cyclizations of 3-substituted 1-(2-cyanophenyl)-thioureas to corresponding 3-substituted 4-imino-1,2,3,4-tetrahydroquinazoline-2-thiones was about minutes or tens of minutes [4]. Also in [3] the authors mentioned that the only dissolving of 3-phenyl-1-(2-cyanophenyl)thiourea in cold ethylene glycol monomethyl ether led to the instantaneous cyclization. It seems that this solvent has better solvation effect than that of ethanol as well as the higher boiling temperature which might also make the reaction quicker.

Therefore we decided to carry out the reaction in ethylene glycol monomethyl ether boiling. Compounds *I* and *V*—*X* during 40—180 min cyclized to 3-substituted 4-imino-5,6,7,8-tetrahydrobenzo[*b*]thieno[2,3-*d*]-1,2,3,4-tetrahydropy-

rimidine-2-thiones *XII—XVIII*. Compounds *II—IV* did not change even under 24 h boiling.

The purity of the products *XII—XIX* was checked by TLC on Silufol in the number of eluents mentioned in Experimental. The R_f values of all synthesized compounds were very close to 0 due to their high polarity. The presence of less polar compounds in the products was not observed. The purity of compounds is signalized by the narrow interval of the melting point (usually 1—3 °C) which did not change after repeated crystallization and by the results of elemental analysis.

The fact that 3-isopropyl-, 3-*tert*-butyl-, and 3-cyclohexyl-1-(3-cyano-4,5,6,7-tetrahydrobenzo[*b*]thien-2-yl)thioureas did not enter into the cyclization reaction could be explained similarly as in [4] by the steric hindrance of the nitrogen atom substituted with a branched substituent which should attack the cyano group. The difference in the reactivity between our thioureas and 3-substituted 1-(2-cyanophenyl)thioureas could be explained by the different geometry of the corresponding phenyl and tetrahydrobenzo[*b*]thienyl analogues as well as by the difference in the electron density distribution at the reaction centre, especially at the cyano group.

References

1. Taylor, E. C. and McKillop, A., in *Advances in Organic Chemistry: Methods and Results*. (Taylor, E. C., Editor.) P. 294. Interscience Publishers, New York, 1970.
2. Taylor, E. C. and Ravindranathan, R. V., *J. Org. Chem. 27*, 2622 (1962).
3. Pazdera, P., Nováček, E., and Ondráček, D., *Chem. Papers 43*, 465 (1989).
4. Pazdera, P., Ondráček, D., and Nováček, E., *Chem. Papers 43*, 771 (1989).
5. Pazdera, P., Řezka, M., and Nováček, E., *Chem. Papers 44*, 63 (1990).

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