elemental analysis and IR and ^{1}H NMR spectral data.

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Activative Influence of the Nitro Group in the Cyclization Reactions of the Addition Products of 2-Chloro-5-nitrobenzoyl Isothiocyanate with the Amines and 2-Propanol

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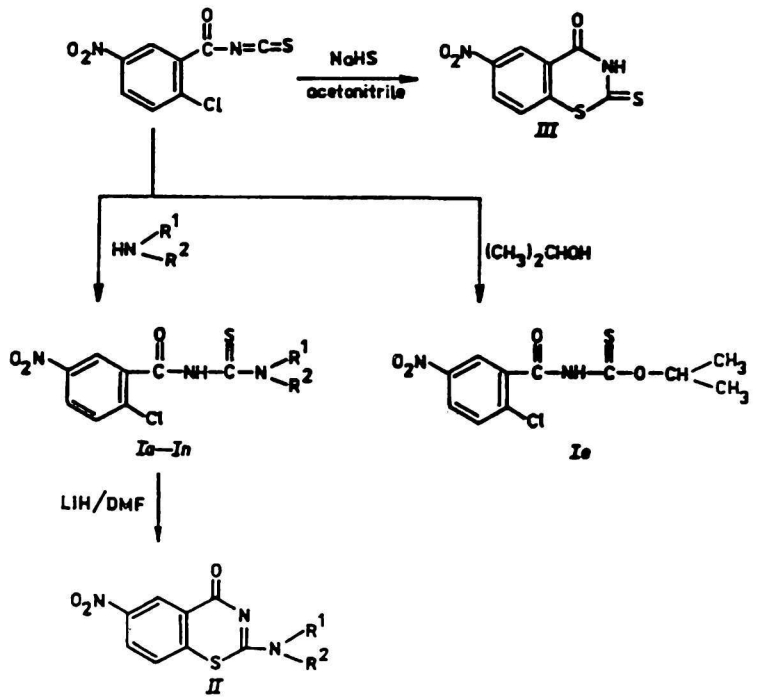
Reaction of 2-chloro-5-nitrobenzoyl isothiocyanate with the primary and secondary alkyl- and arylamines, as well as with 2-propanol yields corresponding thioureas, or *O*-isopropyl monothiocarbamate, respectively. Heating of these thioureas in dimethylformamide with LiH or in the benzene solution of triethylamine leads to formation of the cyclization products, *i.e.* the corresponding 2-alkyl(aryl)amino-6-nitro-4*H*-1,3-benzothiazin-4-ones.

2-Thioxo-6-nitro-2,3-dihydro-4*H*-1,3-benzothiazin-4-one can be obtained by the reaction of 2-chloro-5-nitrobenzoyl isothiocyanate with sodium hydrogen sulfide. The synthesized benzothiazines are stable, their heating or melting does not lead to the rearrangement into the benzopyrimidinic heterocycles.

Studying the cyclization reactions of the products of the addition of 2-chlorobenzoyl isothiocyanate to the amines and alcohols, we came to a conclusion that the cyclization reactions occur only with those thioureas that have been obtained from the primary alkyl- and arylamines [1]. These cyclization reactions result in the derivatives of quinazolinones. Thioureas synthesized from the secondary amines as well as addition products of 2-chlorobenzoyl isothiocyanate with alcohols do not undergo the cyclization reactions. It was interesting to find out what would happen with the nitrogen and oxygen adducts of 2-chlorobenzoyl isothiocyanate that has a nitro group in the position 5. This group has a strong electron-accepting effect on nucleophilicity of the chlorine atom in *para* position of the benzene ring. Such activating influence results in the formation of the benzothiazine derivatives, as well as in the addition-elimination reaction with sodium hydrogen sulfide that produces 2-thioxobenzothiazine *III* (Scheme 1). This effect was utilized by *Deorha et al.* [2, 3] at the preparation of 2,4-dioxobenzothiazines using a reaction of the ester of 2-chloro-5-nitrobenzoic



Scheme 1

acid with *N*-substituted thiourea. Benzothiazine derivatives with different degree of saturation were synthesized using various methods [4—7].

Biological activity of the benzothiazine derivatives is very diverse. The compounds of this type are known to serve as psychostimulators, antidepressants, analgetics, bacteriostatics, fungicides, antipyretics, sedatives, and spasmolytics [8].

2-Chloro-5-nitrobenzoyl isothiocyanate synthesized using a rhodanide method has not been so far described in the literature. It is a solid crystalline substance that is stable at the ambient temperature. The synthesized thioureas *Ia—In* (Table 1) as well as benzothiazines *II* (Table 2) are very poorly soluble in organic solvents. This fact caused some problems at measuring and interpretation of their IR and ^{13}C NMR spectra. Therefore, only five benzothiazines have been identified.

The structures of the obtained thioureas *Ia—In*, of the isopropyl ester *Io* and benzothiazines *II* were confirmed by their IR and ^1H NMR spectra, and the benzothiazine derivatives were identified by their mass spectra containing a common fragment with m/z = 181 that proves the benzothiazine skeleton (Scheme 2).

The synthesized benzothiazine derivatives are stable even at 200 °C that implies high stability of the condensed skeleton of the molecule. Reaction of the *O*-isopropyl monothiocarbamate *Io* with LiH in DMF did not produce a corresponding 2-*O*-isopropyl-1,3-benzothiazine, but yielded nonisolable degradation products. We suggest that in alkaline medium a scission of the isopropyl residue occurred, as well as the degradation of the thiocarbamic group without cyclization.

In the IR spectra of thioureas *Ia—In* (Table 3) the ν(C=O) vibrations lie at $\tilde{\nu} \approx 1670$ cm^{-1}, which is higher than the corresponding value with 2-alkyl-(aryl)amino-4*H*-1,3-benzothiazin-4-ones (Table 4), where ν(C=O) vibrations lie in the region of $\tilde{\nu}$ = 1630—1645 cm^{-1}. The stretching vibrations ν(NH—C=S) are present as a typical broad band at $\tilde{\nu}$ = 1510—1520 cm^{-1}. In benzothiazine derivatives this band disappears and a new band corresponding to ν(C=N) emerges in the region about 1600 cm^{-1}. In the IR spectrum of 2-thioxo-6-nitro-2,3-dihydro-4*H*-1,3-benzothiazin-4-one we can observe ν(C=O) vibrations at $\tilde{\nu}$ = 1700 cm^{-1}. The vibrations of the nitro group are located as could be expected at 1600—1630 cm^{-1}.

EXPERIMENTAL

IR spectra were measured using Specord 75 spectrophotometer (Zeiss, Jena) in KBr tablets, ^1H NMR spectra using a BS-487A (80 MHz) spectrometer (Tesla). The samples were dissolved in the $CDCl_3$—DMSO-d_6 mixture with TMS as an internal standard. ^{13}C NMR and UV spectra have not been measured due to low solubility of the nitro derivatives of thioureas and benzothiazines. Mass spectra were measured using IMS-100D mass spectrometer (Jeol) at ionization energy 70 eV and the following temperatures of the ionization chamber: 225 °C (*IIm*), 240 °C (*IIi*, *IIn*), 265 °C (*IIe*), 150 °C (*III*). The reaction course was followed

Table 1. Characterization of the *N*-Alkyl(aryl)- and *N,N*-Dialkyl(diaryl)-*N'*-(2-chloro-5-nitrobenzoyl)thioureas

Compound	R^1	R^2	Formula	M_r	w_i(calc.)/% w_i(found)/%			Yield/%	M.p./°C
					C	H	N		
Ia	H	H	$C_8H_6ClN_3O_3S$	259.6	37.01 37.03	2.33 2.36	16.18 16.20	72	144—145
Ib	H	C_2H_5	$C_{10}H_{10}ClN_3O_3S$	287.6	41.76 41.56	3.50 3.58	14.61 14.70	64	157—158
Ic	H	C_6H_5	$C_{14}H_{10}ClN_3O_3S$	335.6	50.10 50.16	3.00 3.04	12.52 12.60	68	163—164
Id	H	$CH_2C_6H_5$	$C_{15}H_{12}ClN_3O_3S$	348.6	51.68 51.71	3.47 3.52	12.05 12.09	74	168—169
Ie	H	3-CH_2—C_5H_3N	$C_{14}H_{10}ClN_4O_3S$	349.6	48.10 48.15	2.88 2.90	16.02 16.12	74	154—155
If	H	$CH_2CH_2C_6H_5$	$C_{16}H_{14}ClN_3O_3S$	362.6	52.99 52.80	5.37 5.40	11.58 11.60	72	151—152
Ig	H	4-CH_3O—C_6H_4	$C_{15}H_{12}ClN_3O_4S$	365.6	49.27 49.30	3.30 3.28	11.49 11.52	62	141—142
Ih	H	4-Cl—C_6H_4	$C_{14}H_9Cl_2N_3O_3S$	370.1	45.43 45.50	2.45 2.50	11.35 11.38	70	169—171
Ii	H	4-NO_2—C_6H_4	$C_{14}H_9ClN_4O_5S$	380.6	44.18 44.20	2.38 2.40	14.72 14.80	67	181—182
Ij	H	2-CH_3-4-Cl—C_6H_3	$C_{15}H_{11}Cl_2N_3O_3S$	384.1	46.90 46.82	2.88 2.90	10.94 11.01	64	172—173
Ik	C_2H_5	C_2H_5	$C_{12}H_{14}ClN_3O_3S$	315.6	45.66 45.70	4.47 4.51	13.31 13.38	68	121—122
Il	—$(CH_2)_4$—		$C_{13}H_{12}ClN_3O_3S$	327.6	47.66 47.71	3.69 3.72	12.82 12.74	71	186—187
Im	—$(CH_2)_2O(CH_2)_2$—		$C_{12}H_{12}ClN_3O_4S$	329.6	43.72 43.81	3.66 3.70	12.74 12.80	73	182—183
In	C_6H_5	C_6H_5	$C_{20}H_{14}ClN_3O_3S$	411.6	58.36 58.40	3.42 3.51	10.21 10.26	63	158—159
Io	-	-	$C_{11}H_{12}ClN_2O_4S$	303.6	43.51 43.50	3.98 3.88	8.47 8.40	54	148—149

Solvent for all compounds chloroform—hexane (φ_r = 1 1).

by means of thin-layer chromatography on Silufol plates (Kavalier, Votice).

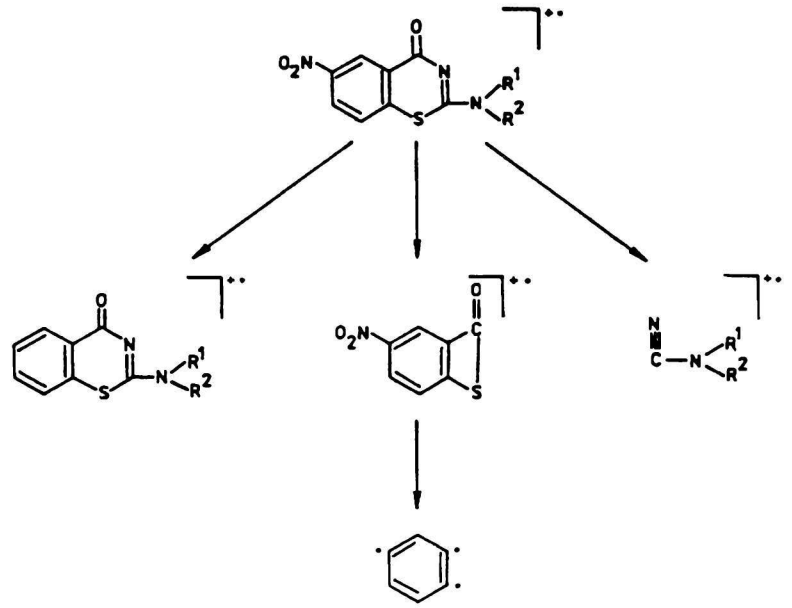
2-Chloro-5-nitrobenzoic acid and its chloride were prepared according to [9] and their physicochemical parameters were in agreement with the literature data.

2-Chloro-5-nitrobenzoyl Isothiocyanate

A mixture of 2-chloro-5-nitrobenzoyl chloride (8.8 g; 0.04 mol), $Pb(SCN)_2$ (13.3 g; 0.04 mol), and hexane (30 cm^3) was moderately refluxed for 1.5 h. Afterwards, a sediment of $PbCl_2$ was removed by filtration. The filtrate was boiled with charcoal, filtered and the solid product was recrystallized from the hexane—petroleum ether (φ_r = 1 : 1) mixture. Melting point of the product was 78 °C, the yield 80 %. For $C_8H_3ClN_2O_3S$ w_i(calc.): 39.58 % C, 1.24 % H, 11.55 % N; w_i(found): 39.60 % C, 1.22 % H, 11.51 % N. IR spectrum, $\tilde{\nu}/cm^{-1}$: 1920 ν(N=C=S), 1700 ν(C=O).

Table 2. Characterization of the 2-Alkyl(aryl)amino-6-nitro-4*H*-1,3-benzothiazin-4-ones

Compound	R^1	R^2	Formula	M_r	w_i(calc.)/% w_i(found)/%			Yield/%	M.p./°C
					C	H	N		
IIe	H	3-CH_2—C_5H_3N	$C_{14}H_{10}N_4O_3S$	314	53.55 53.54	3.21 3.20	17.84 17.83	57	232—233
IIi	H	4-NO_2—C_6H_4	$C_{14}H_8N_4O_5S$	344	48.88 48.83	2.34 2.34	16.28 16.26	53	216—217
IIk	C_2H_5	C_2H_5	$C_{12}H_{13}N_3O_3S$	279	51.62 51.58	4.69 4.72	15.06 15.03	56	223—224
IIm	—$(CH_2)_2O(CH_2)_2$—		$C_{12}H_{11}N_3O_4S$	293	49.15 49.17	3.78 3.80	14.34 17.32	51	224—225
IIn	C_6H_5	C_6H_5	$C_{20}H_{13}N_3O_3S$	375	64.05 64.08	3.49 3.51	11.20 11.22	51	231—232



Scheme 2
Basic fragmentation routes of the 2-alkyl(aryl)amino-6-nitro-4*H*-1,3-benzothiazin-4-ones.

N-Alkyl(aryl)-*N'*-(2-chloro-5-nitrobenzoyl)thioureas *Ia—In* and Isopropyl 2-Chloro-5-nitrobenzoylmonothiocarbamate (*Io*)

2-Chloro-5-nitrobenzoyl isothiocyanate (9.7 g; 0.04 mol) was dissolved in benzene or chloroform and gradually amine or 2-propanol (0.04 mol) was added. After several hours a product precipitated that represented the corresponding thiourea or monothiocarbamic acid ester. The product was separated by filtration, dissolved in chloroform or methanol, boiled with charcoal and recrystallized from the chloroform—hexane or methanol—water mixture.

Table 3. IR and ^{1}H NMR Spectral Data of Compounds *Ia—Io*

Compound	$\tilde{\nu}$/cm^{-1}				δ			
	ν(C=O)	ν(NH)	ν(NH—C=S)	ν(NO_2)	H_{arom}	NH	CH_3	CH_2
Ia	1680	3400	1525	1600 1370	7.9—8.1	9.8—11.8	–	–
Ib	1675	3390	1520	1600 1400	7.9—8.1	8.8 9.2	1.4	3.1
Ic	1680	3380	1510	1610 1395	7.5—8.2	11 11.2	–	–
Id	1675	3390	1520	1600 1400	7.5—8.2	9.7 10.6	–	4.9
Ie	1675	3240	1525	1600 1400	7.8—8.3	8.9 11.1	–	5.1
If	1670	3440	1520	1600 1395	7.5—8.2	9.1 8.9	–	3.0 3.6
Ig	1675	3395	1525	1600 1410	7.5—8.0	9.6 8.7	3.76	–
Ih	1675	3380	1525	1600 1400	7.5—8.1	12.4 12.2	–	–
Ii	1680	3375	1520	1600 1400	7.5—8.2	9.5 11.3	–	–
Ij	1680	3395	1520	1600 1390	7.7—8.4	12 8.7	2.1	–
Ik	1690	3390	1520	1600 1390	8.1—8.3	8.5	1.25	3.75
Il	1685	3370	1520	1600 1400	7.35—8.3	9.1	–	3.75
Im	1690	3365	1520	1600 1400	7.9—8.2	–	–	3.8
In	1680	3390	1510	1600 1390	7.7—8.2	8.7	–	–
Io	1680	3370	1460	1600 1385	7.6—8.2	9.15	1.15	5.45 (CH)

Table 4. IR Spectral Data of Compounds *II*

Compound	$\tilde{\nu}$/cm^{-1}		
	ν(C=O)	ν(C=N)	ν(NO_2)
IIe	1640	1590	1575, 1340
IIi	1650	1595	1570, 1345
IIk	1630	1590	1575, 1330
IIm	1660	1610	1565, 1345
IIn	1645	1600	1570, 1350

2-Alkyl(aryl)amino-6-nitro-4*H*-1,3-benzothiazin-4-ones *IIe*, *IIi*, *IIk*, *IIm*, *IIn*

Compound *Ia*—*In* (0.02 mol) was dissolved in the minimal volume of dimethylformamide and lithium hydride (0.12 g; 0.015 mol) was added. Reaction mixture was moderately refluxed for 1.5 h. Then water (15 cm^3) was added and the solution was neutralized with diluted HCl (φ_r = 1 1). The precipitated cyclic product was filtered and recrystallized from the methanol—water or chloroform—hexane mixture.

2-(3-Picolylamino)-6-nitro-4H-1,3-benzothiazin-4-one (*IIe*); Mass spectrum, *m/z* (I_r/%): 314 (20), 181 (40), 107 (36), 92 (100), 75 (60).

2-(4-Nitrophenylamino)-6-nitro-4H-1,3-benzothiazin-4-one (*IIi*); Mass spectrum, *m/z* (I_r/%): 344 (100), 328 (17), 297 (16), 181 (63), 163 (17), 75 (20).

2-Diethylamino-6-nitro-4H-1,3-benzothiazin-4-one (*IIk*); Mass spectrum, *m/z* (I_r/%): 279 (30), 184 (100), 181 (31), 110 (20), 75 (46).

2-Morpholino-6-nitro-4H-1,3-benzothiazin-4-one (*IIm*); Mass spectrum, *m/z* (I_r/%): 293 (12), 181 (100), 112 (85), 110 (90), 75 (68).

2-Diphenylamino-6-nitro-4H-1,3-benzothiazin-4-one (*IIn*); Mass spectrum, *m/z* (I_r/%): 375 (100), 329 (52), 194 (82), 181 (15), 77 (81), 75 (18).

2-Thioxo-6-nitro-2,3-dihydro-4*H*-1,3-benzothiazin-4-one (*III*)

2-Chloro-5-nitrobenzoyl isothiocyanate (5 g; 0.02 mol) was dissolved in acetonitrile (20 cm^3) and NaHS (1.15 g; 0.02 mol) was added. Reaction mixture was refluxed for 2.5 h. Afterwards water (15 cm^3) was added and the mixture was neutralized with diluted HCl (φ_r = 1 1). The precipitated cyclic product was separated by filtration and recrystallized from methanol—water or chloroform—hexane.

Yield = 71 %, m.p. = 149—150 °C. For $C_8H_4N_2O_3S_2$ w_i(calc.): 40.01 % C, 1.66 % H, 11.66 % N; w_i(found): 40.15 % C, 1.69 % H, 11.70 % N. IR spectrum, $\tilde{\nu}$/cm^{-1}: 1635 ν(C=O), 1570, 1340 ν(NO_2), 1510 ν(NH—C=S). Mass spectrum, *m/z* (I_r/%): 240 (23), 181 (100), 138 (20), 75 (70).

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