2-Oxo-8-methylthio-6-phenyl-1,2-dihydrothiazolo[3,4-a]thiazolo[5,4-e]pyrimidinium Benzenesulfonate and Perchlorate (IIIa,b, Table 1). A mixture of 0.76 g (2 mmole) of benzenesulfonate I, 0.32 g (2 mmole) of aldehyde II, and 2 ml of acetic acid was heated at 100°C for 1 h, after which the precipitated benzenesulfonate (IIIa) was removed by filtration and crystallized from DMF to give 0.5 g of product. The perchlorate (IIIb) was obtained by adding 0.5 ml of 72% perchloric acid to the reaction mixture prior to cooling. It was crystallized from alcohol–DMF (1:1).

6-Phenyl-8-[(3-ethyl-2-benzothiazolinylidene)methyl]thiazolo[3,4-a]thiazolo[5,4-e]pyrimidinium 2-Oxide (IV). A mixture of 0.43 g (1 mmole) of salt IIIa and 0.35 g (1 mmole) of 2-methyl-3-ethylbenzothiazolium toluenesulfonate in 5 ml of absolute alcohol and 3 ml of DMF was heated to the boiling point, and 0.2 g (2 mmole) of triethylamine was added. Dye IV was removed by filtration and crystallized from alcohol–DMF (1:1). The yield was 0.3 g.

6-Phenyl-8-[(1-ethyl-1,4-dihydroquinolin-4-ylidene)methyl]thiazolo[3,4-a]thiazolo[5,4-e]-pyrimidinium 2-Oxide (V). A mixture of 0.43 g (1 mmole) of salt IIIa and 0.27 g (1 mmole) of 4-methyl-1-ethylquinolinium perchlorate was dissolved by heating in 5 ml of absolute alcohol and 2 ml of DMF, after which 0.2 g (2 mmole) of triethylamine was added. Dye V was removed by filtration and crystallized from alcohol–DMF (1:1). The yield was 0.25 g.

2-Oxo-6-phenyl-8-[(3-ethyl-2-benzothiazolinylidene)methyl]1,2-dihydrothiazolo[3,4-a]thiazolo[5,4-e]pyrimidinium Perchlorate (IV). This compound was obtained by adding excess 72% perchloric acid to a solution of dye IV in alcohol–DMF (1:1).

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SYNTHESIS AND PHYSICOCHEMICAL PROPERTIES OF THIAZOLINO[3,2-a]BENZIMIDAZOLES

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UDC 547.785.5'789.07:543.422.51

The reaction of 1-β-hydroxyalkyl(aralkyl)-2-chlorobenzimidazoles with thiourea or the reduction of 1-acylmethylbenzimidazoline-2-thiones with sodium borohydride gave 1-β-hydroxyalkyl(aralkyl, hetaryl)benzimidazoline-2-thiones, which were converted to 2-alkyl(aryl, hetaryl)-substituted thiazolino[3,2-a]benzimidazoles by the action of $POCl_3$.

The antispasmodic activity of 2,3-dihydrothiazolo[3,2-a]benzimidazole derivatives is known [1, 2]. In a continuation of our search for preparations of this series of compounds with the indicated activity [3, 4] we isolated 1-β-hydroxyalkyl(aralkyl)benzimidazoline-2-thiones (IIIa,c,d,f, Table 3), which were obtained by the reaction of the corresponding 1-β-hydroxyalkyl(aralkyl)-2-chlorobenzimidazoles (Ia,c,d,f) [5] with thiourea in methanol (ethanol). Substances IIIb,e,g were synthesized by the reduction of 1-acylmethylbenzimidazoline-2-thiones (IIb,e,g) [6] with sodium borohydride in an aqueous alcohol medium. 2-Alkyl(aryl,

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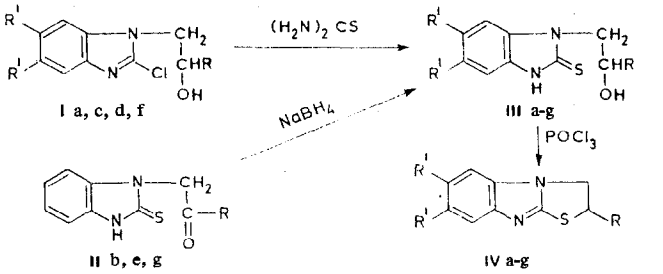
0009-3122/83/1907-0756$07.50

TABLE 1. PMR Spectra of IIIa,b,g

Compound	Solvent	Chemical shifts, ppm						SSCC (Hz)		
		NH	H_{arom}	CH_2	CH	OH	R	J_{1H^1-2H}	J_{1H^2-2H}	$J_{1H^1-1H^2}$
IIIa	d_6-DMSO	—	7,15—7,57 m (with a max. at 7.26-7.46)	4,23± ±0,02m	3,96± ±0,02 q	1,50	1,00d	2	11	16
IIIb	C_6D_6	9,37s	6,50—7,02 m (with a max.at 6,98)	4,11± ±0,02m	3,58± ±0,02 q (w/a max. 3,63 and 3,53)	2,28d	0,94s	3	10	15
IIIg	CD_3CD_2OD	9,24 s	6.94—7,42 m (w/a max. at 7.29 and 7.09)	4,58± ±0,02m	5,66± ±0,02 q	—	6,94— 7,42m	5	8	14

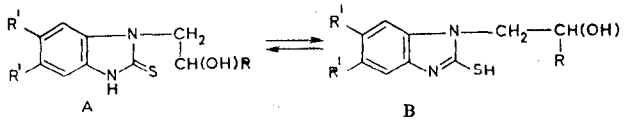
hetaryl)-thiazolino[3,2-a]benzimidazoles (IVa-g, Table 3) were obtained in good yields by treatment of thiones IIIa-g with phosphorus oxychloride [without isolation of the intermediate 1-β-chloroalkyl(aralkyl, hetaryl)benzimidazoline-2-thiones].

The IR spectroscopic data do not make it possible to speak with confidence regarding the existence of thione—thiol tautomerism in IIIa-g. In the IR spectra we did not observe νSH absorption bands at ∿2500 cm^{-1}, and it was too difficult to make accurate assignments in the "fingerprint" region (νC=S = 1300-1400 cm^{-1} and νSH = 920-1100 cm^{-1}) because of pronounced overlapping of the absorption bands. The rather broad absorption band at 3200-3400 cm^{-1} can be assigned to vibrations of the NH and/or OH groups tied up in a hydrogen bond.



a R=CH_3, R'=H; b R=$C(CH_3)_3$, R'=H; c R=C_6H_5, R'=H; d R=4-$O_2NC_6H_4$, R'=H; e R=4-$CH_3OC_6H_4$, R'=H; f R=4-$O_2NC_6H_4$, R'=CH_3; g R=α-C_4H_3S, R'=H

The PMR spectra of IIIa-g are rather complex because of the presence of an asymmetric center (an AA'X system). An analysis of them (Table 1) provides evidence in favor of structure A, although the signal of the proton of the NH group is not always recorded in the spectra even in d_6-DMSO.



The methylene protons are recorded in the form of a multiplet complicated by vicinal and geminal splitting. The signal of the methylidyne group is usually a poorly resolved quartet (for IIIb,g) or a multiplet. In the case of IIIb a broad doublet of a hydroxy group centered at 2.28 ppm is recorded in the spectrum. The ratios of the areas of the signals are as follows: H_{arom}:CH_2:CH:OH:CH_3 = 4:2:1:1:3 (IIIa); NH:H_{arom}:CH_2:CH:OH:$C(CH_3)_3$ = 1:4:2:1:1:9 (IIIb); NH:H_{arom}:CH_2:CH = 1:7:2:1 (IIIg).

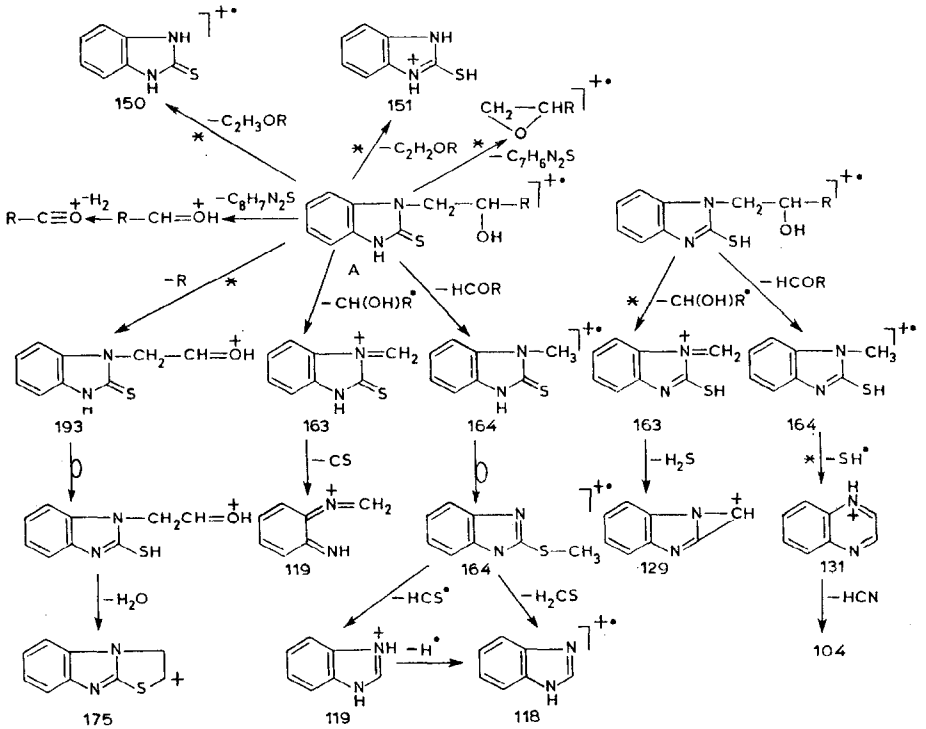
In a previous study [7] of the fragmentation of 1-β-hydroxyalkyl(aralkyl)-2-chlorobenzimidazoles under the influence of electron impact (structural analogs of the compounds under consideration) it was shown that α cleavage of the C—C bond relative to the hydroxy group is

TABLE 2. Principal Ion Peaks in the Mass Spectra of III and IV (in percent of the maximum peak in the mass spectra)

Ions, m/z	Compound			Ions, m/z	Compound		
	IIIa	IIIb	IIIg		IVa	IVb	IVg
M^+	26,0	49,4	26,5	M^+	100,0	93,3	80,0
193	5,0	21,2	3,0	$[M-H]^+$	14,4	1,4	8,3
175	11,0	8,8	—	$[M-R]^+$	36,0	100,0	17,0
164	6,4	18,2	17,6	$[M-SH]^+$	14,0	3,4	12,0
163	5,4	21,2	18,2	161	20,0	8,5	3,5
151	100,0	100,0	100,0	150	11,4	33,1	100,0
150	40,6	91,7	88,2	129	6,8	9,3	11,0
131	7,2	21,2	11,2	118	8,8	22,0	11,0
129	3,3	6,8	5,5	117	11,6	24,6	6,5
119	8,8	34,1	20,6	103	20,0	7,3	11,2
118	12,0	16,5	9,4	102	10,0	8,5	10,2
104	8,4	7,4	7,8	RCH_2^+	10,3	4,6	23,8
$RCH{=}\overset{+}{O}H$	5,3	7,4	7,8	$RH^{+\cdot}$	18,2	5,3	6,3
RCO^+	7,7	—	7,8	R^+	15,3	4,5	2,5
$RCH(OH){=}\overset{+}{C}H$	6,0	3,1	17,8				

realized in such systems (it was assumed that the charge in the M^+ molecular ion is concentrated on the oxygen atom). These processes are accompanied by migration of a hydrogen atom from the hydroxy group (proved by means of deuterium labeling) to the site of cleavage. In our case a similar process also takes place (ion peaks with m/z* 163, 164, and 193, $RCH{=}\overset{+}{O}H$ and R^+), which confirms the presence of a substituent in the 1 position of the benzimidazoline-2-thione molecule (Scheme 1).

Scheme 1



Another pathway of the fragmentation of M^+ involves cleavage of the C–N bond and is also accompanied by migration of hydrogen atoms (ion peaks at 150 and 151). The peaks of ions with masses of 150 and 151, which are formed as a result of the usual β cleavage relative to the aromatic ring, are the most intense peaks in the spectra of IIIa,b,g and constitute evi-

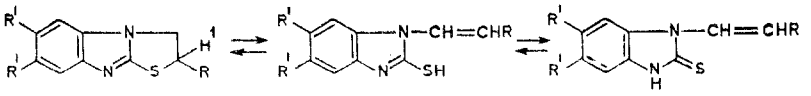
*Here and subsequently in the text and in the schemes, the numbers that characterize the ions are the mass-to-charge ratios (m/z).

dence that in this case the charge in M^+ is primarily localized in the phenylene part of the molecule; the formation of the ion with m/z 151 may be due to only the thiol form of M^+ (this constitutes an indirect indication of the existence of a hydrogen bond within the molecule [8, 9]).

The subsequent fragmentation of the ion with m/z 164 suggests the possibility of the existence of two tautomers [10]. The formation of an ion with m/z 129 is also due to the thiol form and the manifestation of an "ortho effect" [9, 11].

Scheme 1 illustrates the overall pattern of the fragmentation of the M^+ ions of IIIa,b,g. The intensities of the principal characteristic ion peaks in their mass spectra are presented in Table 2.

The cyclization of 1-β-hydroxyalkyl(aralkyl, hetaryl)-substituted benzimidazoline-2-thiones (IIIa-g) may proceed with tautomeric transformations of the following form (C ⇄ D ⇄ E, IVa-g):



C D E

In order to determine the predominant form of the tautomer we used the methods of physicochemical analysis indicated above.

The IR spectra of IVa-g do not contain the absorption bands of SH, NH, and C=S groupings. These data make it possible to draw a preliminary conclusion that the D and E tautomeric forms are not realized. More rigorous proof for this assumption can be obtained on the basis of a study of the PMR spectra.

Thus for IVa the distribution of the integral intensities of the signals of the protons corresponds to 4:2:1:3, which corresponds to the C form (H_{arom}:CH_2:CHR:CH_3). In addition, signals of protons of the NH group were not observed in the weak-field part of the spectrum. The aromatic protons of the benzimidazole part of the molecule show up in the form of a complex multiplet at 6.98-7.85 ppm. The methylene grouping, which consists of nonequivalent protons (an ABX system), forms a multiplet at 4.15-4.65 ppm. The proton of the methylidyne group gives a signal in the form of a quartet with a maximum at δ 3.72 and 3.77 ppm ($J_{H^1,R}$ = 7.0 Hz). The methyl group appears as a doublet centered at 1.63 ppm with J_{R,H^1} = 7.0 Hz.

The PMR spectrum of IVb is a complex pattern in connection with superimposition of the 1-H signal (a triplet) on the signals of the protons of the methylene group (an AA'X system), which is recorded in the form of a multiplet, the components of which are complicated by geminal and vicinal splitting. This set of signals is found at 3.78-4.35 ppm and is centered at 4.06 ppm. The signals of the aromatic protons of the benzimidazole part of the molecule lie at 6.95-7.58 ppm. The distribution of the integral intensities corresponds to the ratio 4:3:9. Thus IVb has structure C in this case also.

Signals of the following protons are observed in the PMR spectrum of a sample of IVg: 1) 1-H in the form of a triplet with δ 5.67, 5.75, and 5.83 ppm; 2) the methylene group is recorded in the form of a complex multiplet at 4.02-4.64 ppm, just as in the preceding cases; 3) the aromatic protons of the benzimidazole part and substituent R appear as a multiplet at 6.82-7.64 ppm (the protons in the β position of thiophene show up at δ 7.18-7.24 ppm; the α proton gives a signal with δ 6.82-6.95 ppm). The ratio of the integral intensities in this case is 7:1:2. Signals of protons of the NH group were not observed in the weak-field part of the spectrum.

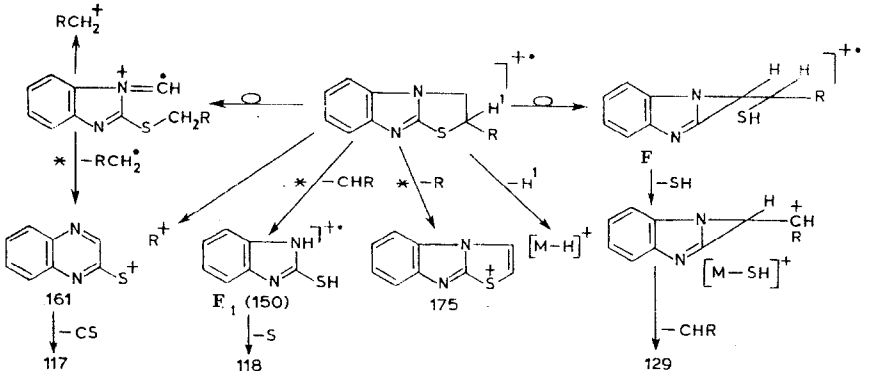
Thus an analysis of the PMR spectra of IV indicates realization of the C structure.

The molecular ions in the mass spectra of IVa,b,g are more stable (by a factor of approximately two to four) than the corresponding III, which also confirms a stable cyclic form of the molecule. The fragmentation of M^+ is realized via pathways that are common to samples of IVa,b,g and constitutes evidence that they belong to a common structural type, excluding the phenomenon of tautomerism.

TABLE 3. Characteristics of the Compounds Obtained

Compound	R	R′	mp, deg C	IR spectrum, cm^{-1}		Found, %				Empirical formula	Calculated, %				Yield, %
				NH	OH	C	H	N	S		C	H	N	S	
IIIa	CH_3	H	163—164		3360—3290	57,2	5,6	13,6	15,6	$C_{10}H_{12}N_2OS$	57,7	5,8	13,5	15,4	76
IIIb	$C(CH_3)_3$	H	175—176	3060	3288	62,2	7,1	11,5	12,8	$C_{13}H_{18}N_2OS$	62,2	7,2	11,2	12,8	86
IIIc	C_6H_5	H	199—200		3400—3315	66,8	5,4	10,3	12,0	$C_{15}H_{14}N_2OS$	66,6	5,2	10,4	11,9	92
IIId	4-$O_2NC_6H_4$	H	219—220		3353	56,9	4,2	13,1	10,0	$C_{15}H_{13}N_3O_3S$	57,1	4,2	13,3	10,2	99
IIIe	4-$CH_3OC_6H_4$	H	182—183	3110	3180	63,5	5,1	9,5	10,3	$C_{16}H_{16}N_2O_2S$	64,0	5,4	9,3	10,7	88
IIIf	4-$O_2NC_6H_4$	CH_3	265—266		3360	59,6	4,9	12,3	9,7	$C_{17}H_{17}N_3O_3S$	59,5	5,0	12,2	9,3	73
IIIg	α-C_4H_3S	H	159—160	3145	3200—3100	57,0	4,8	10,5	22,8	$C_{13}H_{12}N_2OS_2$	56,5	4,4	10,1	23,2	77
IV[a]	CH_3	H	123—124			63,4	5,1	14,5	16,4	$C_{10}H_{10}N_2S$	63,1	5,3	14,7	16,9	87
IVb	$C(CH_3)_3$	H	135—136			66,9	7,0	12,0	13,7	$C_{13}H_{16}N_2S$	67,2	6,9	12,1	13,8	86
IVc	C_6H_5	H	132—133			71,3	5,0	10,9	13,0	$C_{15}H_{11}N_2S$	71,4	4,8	11,1	12,7	90
IVd	4-$O_2NC_6H_4$	H	190—191			60,9	4,0	14,0	10,5	$C_{15}H_{10}N_3O_3S$	60,6	3,7	14,1	10,8	91
IVe	4-$CH_3OC_6H_4$	H	119—121			68,5	5,1	10,8	11,8	$C_{16}H_{14}N_2OS$	68,1	5,0	9,9	11,4	95
IVf	4-$O_2NC_6H_4$	CH_3	177—178			63,2	4,6	13,1	9,7	$C_{17}H_{14}N_3O_2S$	62,7	4,6	12,9	9,9	92
IVg	α-C_4H_3S	H	134—135			60,1	3,8	11,5	25,0	$C_{13}H_{10}N_2S_2$	60,4	3,9	11,8	24,8	95

Scheme 2



The fragmentation of M^+ is realized via several characteristic pathways that are specific for cyclic amines [12-14] and thiophene [15]. The primary pathway is splitting out of the 1-H atom and/or the R substituent (β cleavage relative to the sulfur atom) and ejection of an $HS^\bullet$ particle [11]. Ogura and co-workers [11] were unable to explain this phenomenon, although, in our opinion, this is the result of skeletal rearrangement of the M^+ ions (the F form), which they also assumed. This is followed by ring opening at the $C_{(2)}-C_{(3)}$ bond. In general form the fragmentation of the M^+ ions of IVa,b,g can be described by Scheme 2.

The subsequent course of the fragmentation of this ion provides evidence for the formation of F_1 ions with a 2-mercaptobenzimidazole structure [16, 17]. The formation of the ions with m/2 102 and 103 is due to the ion with m/z 129, which has the structure of a pseudomolecular quinoline ion [11]. The intensities of the principal characteristic ion peaks in the mass spectra of IVa,b,g are presented in Table 2.

EXPERIMENTAL

The IR spectra of KBr pellets of the compounds were recorded with a UR-10 spectrometer. The PMR spectra of solutions in d_6-DMSO were obtained at 25°C with an HA-100D spectrometer with hexamethyldisiloxane as the internal standard. The mass spectra were recorded with an MAT-311 spectrometer under standard conditions: The ionizing voltage was 70 eV, the cathode emission current was 300 μA, the accelerating voltage was 3 kV, and the temperature of the source was 150°C.

The 1-β-hydroxyalkyl(aralkyl)-2-chlorobenzimidazoles (Ia,c,d,f) were obtained by the method in [5]; their constants were in agreement with the literature data. The 1-acylmethylbenzimidazoline-2-thiones (IIb,e,g) were obtained by the method in [6].

1-β-Hydroxyalkyl(aralkyl, hetaryl)benzimidazoline-2-thiones (IIIa-g). A) A 1.52-g (0.02 mole) sample of thiourea and one to two drops of 48% HBr were added to a solution of 0.01 mole of 1-β-hydroxyalkyl(aralkyl)-2-chlorobenzimidazole (Ia,c,d,f) in 30-60 ml of methanol (ethanol), and the reaction mixture was refluxed for 2-3 h. The solvent was removed by distillation *in vacuo*, and the residue was dissolved in 50-60 ml of 10% KOH solution. The solution was filtered, the filtrate was neutralized with CH_3COOH solution, and the precipitate (IIIa) was removed by filtration. In the preparation of IIIc,d,f the reaction mixture was cooled and poured into water, the aqueous mixture was neutralized with $NaHCO_3$, and the precipitate was removed by filtration.

B) A 0.2-g sample of KOH was dissolved in 20-30 ml of ethanol, 0.01 mole of 1-acylmethylbenzimidazoline-2-thione (IIb,e,g) and 0.4 g of $NaBH_4$ were added, and the mixture was maintained at 18-20°C for 22-24 h. It was then poured into water, the aqueous mixture was neutralized to pH 6 with CH_3COOH solution, and the precipitate (IIIb,e,g) was removed by filtration.

2-Alkyl(aryl, hetaryl)thiazolino[3,2-a]benzimidazoles (IVa-g). A 15-20-ml sample of freshly distilled $POCl_3$ was added to 0.01 mole of 1-β-hydroxyalkyl(aralkyl, hetaryl)benzimidazoline-2-thiones (IIIa-g), and the mixture was heated in a stainless steel autoclave at 150-155°C for 3 h. It was then cooled, the $POCl_3$ was removed by vacuum distillation, and the residue was decomposed with ice water and hydrolyzed with ammonium hydroxide, and the precipitate was removed by filtration.

Compounds IIIa-g and IVa-g were colorless, yellow (IIId,f and IVd,f), or light-brown (IIIg and IVe) crystalline substances that were soluble in most organic solvents. The compounds were purified for analysis by crystallization from water (IIIa, IVa), ethanol (IIIb,e and IVd,f), aqueous methanol (IVb,c), acetone (IIId), aqueous acetone (IVe,g), aqueous DMF (IIIf), or benzene (IIIg).

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