Bis(3-phenyl-4-oxo-3,4,5,6,7,8-hexahydrobenzo[b]thieno[2,3-d]pyrimidin-2-yl) Disulfide (Va). A 4.18-g (10 mmole) sample of IIa was dissolved in 50 ml of CCl$_4$, and a solution of 0.8 g (5 mmole) of bromine in 20 ml of CCl$_4$ was added dropwise with constant stirring at room temperature. The resulting precipitate was separated and washed successively with 5 ml of water and 1 ml of alcohol.

Compound Va was also obtained in quantitative yield via a similar method by bromination of Ia, IIIa, and IVa.

Bis(3-allyl-4-oxo-3,4,5,6,7,8-hexahydrobenzo[b]thieno[2,3-d]pyrimidine-2-yl) Disulfide (Vb). This compound was obtained in quantitative yield by bromination of IIb, IIIb, and IVb by the method used to prepare Va.

Compound Vb, with mp 179-181°C, was previously synthesized via an independent method [8].

2-Piperidyl-3-phenyl-4-oxo-3,4,5,6,7,8-hexahydrobenzo[b]thieno[2,3-d]pyridimine (VI). A mixture of 1.72 g (20 mmole) of piperidine, 0.62 g (1 mmole) of Va, and 2 ml of methanol was heated on a boiling-water bath for 10 min, after which the precipitated sulfur was removed from the hot solution by filtration. The filtrate was cooled to precipitate VI.

The 2-amino derivatives (VII-X) of thieno[2,3-d]pyrimidines were synthesized from disulfides Va, b and the corresponding amines as in the preparation of VI.

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SYNTHESIS AND PROPERTIES OF 5-(5-NITRO-2-FURYL)THIAZOLINES

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The reactions of 2-amino-4-methyl-5-(5-nitro-2-furyl)thiazole with excess methyl iodide leads to 3,4-dimethyl-2-methylamino-5-(5-nitro-2-furyl)thiazolium iodide, which is converted to 2-imino-3,4-dimethyl-5-(5-nitro-2-furyl)thiazoline under the influence of bases. The iminothiazoline structure was proved by comparison of the spectral characteristics of its acetyl derivative and the isomeric 2-(N-acetyl-N-methyl)amino-4-methyl-5-(5-nitro-2-furyl)thiazole. The pK$_a$ values of 2-amino-4-methyl-5-(5-nitro-2-furyl)thiazole and 3,4-dimethyl-2-imino-5-(5-nitro-2-furyl)-thiazoline were determined, and the constant of the aminothiazole—iminothiazoline tautomeric equilibrium was calculated.

In a previous communication [1] we showed that 2-amino-5-(5-nitro-2-furyl)thiazoles react with carboxylic acid anhydrides exclusively at the exocyclic amino group.

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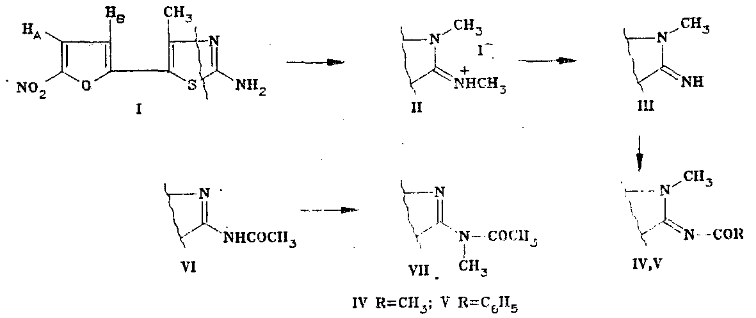
TABLE 1. Spectral Characteristics of the Synthesized II-V and VII

Compound	Electronic spectrum, λ_{max}, nm (log ε)	IR spectrum, cm⁻¹	PMR spectrum, δ, ppm (J, Hz) furan H_A	furan H_B	4-CH_3	other protons
II	220 (4,35), 275 (3,93), 373 (4,17)	3230 (NH)	7,44 (d, 1H, 4,0)	6,72 (d, 1H, 4,0)	2,55 (s, 3H)	3,22 (s, 3H, 3-CH_3), 3,71 (s, 3H, 2-NCH_3)
III	210 (3,98), 296 (4,05), 447 (4,18)	3320 (NH)	7,34 (d, 1H, 4,0)	6,64 (d, 1H, 4,0)	2,37 (s, 3H)	3,59 (s, 3H, 3-CH_3)
IV	225 (3,93), 275 (4,02), 315 (3,93), 405 (4,20)	1615 (C=O)	7,15 (d, 1H, 4,0)	6,57 (d, 1H, 4,0)	2,40 (s, 3H)	3,75 (s, 3H, 3-CH_3), 2,23 (s, 3H, $COCH_3$)
V	245 (4,05), 275 (3,78), 340 (3,98), 403 (4,20)	1618 (C=O)	7,14 (d, 1H, 4,0)	6,63 (d, 1H, 4,0)	2,40 (s, 3H)	3,80 (s, 3H, 3-CH_3), 7,1—7,5 (m, 5H, C_6H_5)
VII	225 (3,98), 300 (3,90), 408 (4,18)	1650 (C=O)	7,15 (d, 1H, 4,0)	6,57 (d, 1H, 4,0)	2,37 (s, 3H)	2,31 (s, 3H, $COCH_3$), 3,53 (s, 3H, CH_3NCO)

In the present research we examined the reaction of 2-aminothiazole I with a "soft" electrophile in the case of the reaction with methyl iodide. Aminothiazole I reacts with excess methyl iodide in acetonitrile to give high-melting salt II with the composition $C_{10}H_{12}N_3O_3SI$.

According to the PMR spectrum (Table 1), II has three magnetically nonequivalent methyl groups, one of which is located in the 4 position of the thiazole ring (singlet at 2.55 ppm). It is not possible to determine the positions of the two methyl groups introduced into the molecule from the PMR data. Crystals of III with the composition $C_9H_9N_3O_3S$, the PMR spectrum of which contains two singlets of methyl groups, precipitate when alkali is added to an aqueous solution of salt II. That is, instead of the expected splitting out of Hl from salt II, CH_3I is eliminated.



Refluxing of III with acetic anhydride leads to monoacetyl derivative IV with the composition $C_{11}H_{11}N_3O_4S$. Compound III also reacts with benzoyl chloride in pyridine to give monobenzoylation product V.

We obtained N-acetyl-N-methylaminothiazole VII, which is isomeric with respect to acetyl derivative IV, by methylation of 2-acetamidothiazole VI in a suspension medium by the method in [2].

A comparison of the spectral characteristics of IV and VII (Table 1) makes it possible to unambiguously establish the structure of acetyl derivative IV. The IR spectrum of amide VII contains the usual "amide I" absorption band at 1650 cm^{-1}, whereas in the case of IV the band of carbonyl absorption is found at 1615 cm^{-1}, which is characteristic for acyl imides [3]. The most substantial differences in the isomers are displayed in the mass spectra (Fig. 1). Fragmentation of the molecular ion with the ejection of ketene and the formation of an $(M - CH_2CO)^{+\bullet}$ cation radical is characteristic for amide VII. The molecular ion of IV undergoes fragmentation as a typical acyl imide [3]. The C—C bond between the carbonyl group and the hydrocarbon residue is cleaved, and the hydrocarbon residue is eliminated in the form of a radical; in our case a methyl radical is split out to give the $(M - CH_3)^+$ cation, the peak of which has the maximum intensity in the mass spectrum of IV.

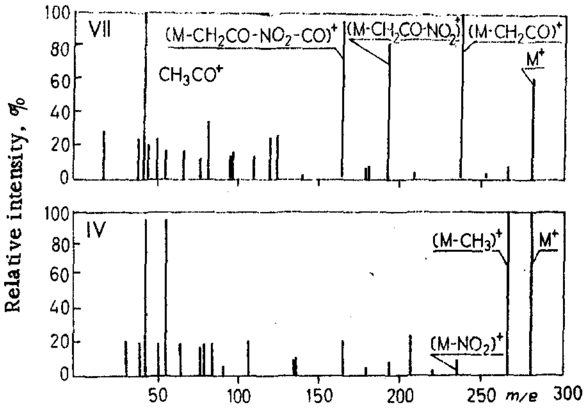


Fig. 1. Mass spectra of IV and VII.

Thus the spectral data constitute unambiguous evidence that IV is 2-acetamido-3,4-dimethyl-5-(5-nitro-2-furyl)thiazoline and, consequently, that II and III have 3,4-dimethyl-2-methylamino-5-(5-nitro-2-furyl)thiazolium iodide and 3,4-dimethyl-2-imino-5-(5-nitro-2-furyl)-thiazoline structures, respectively.

The spectrophotometrically determined pK_a values for aminothiazole I and iminothiazoline III (model of the imino form used for the determination of the aminothiazole—iminothiazoline tautomeric equilibrium [3-5]) are 3.62 ± 0.04 and 7.82 ± 0.05, respectively. Consequently, the tautomeric equilibrium constant for I is $1.6 \cdot 10^4$.

Upon comparing the pK_a and K_t values obtained with the corresponding values of the same constants for unsubstituted 2-aminothiazole (2-aminothiazole has $pK_a = 5.32$ [6], and 3-imino-3-methylthiazoline had $pK_a = 9.6$ [7], $K_t = 2 \cdot 10^4$) it may be concluded that the introduction of a nitrofuran fragment into the 5 position of the thiazole ring leads to a decrease in the basicities of both the amino and imino forms of approximately the same magnitude ($\sim 10^2$). As a result, the tautomeric equilibrium constant remains virtually unchanged on passing from unsubstituted 2-aminothiazole to its 5-nitrofuryl derivative I.

EXPERIMENTAL

The IR spectra of mineral oil suspensions of the compounds were recorded with a UR-20 spectrometer. The electronic spectra of alcohol solutions were obtained with a Specord UV-vis spectrophotometer. The PMR spectra of solutions in CF_3COOH were recorded with a Tesla BS-467 spectrometer with hexamethyldisiloxane (HMDS) as the internal standard. The mass spectra were obtained with a Varian CH-8 high-resolution spectrometer with direct introduction of the samples into the ion source; the temperature of the ionizing chamber was 100-150°C, and the energy of the ionizing electrons was 70 eV.

The characteristics of II-V and VII are presented in Tables 1 and 2.

3,4-Dimethyl-2-methylamino-5-(5-nitro-2-furyl)thiazolium Iodide (II). A 5-ml (81 mmole) sample of methyl iodide was added to a solution of 1 g (4.4 mmole) of aminothiazole I in 50 ml of acetonitrile, the mixture was refluxed for 20-25 h, and 35-40 ml of the solvent was evaporated. Dry ether (50 ml) was added to the residue, and the precipitated yellow crystals of II were washed with 10-15 ml of ether and dried.

3,4-Dimethyl-2-imino-5-(5-nitro-2-furyl)thiazoline (III). A suspension of 1 g (2.6 mmole) of salt II and 0.15 g (2.6 mmole) of KOH in 30 ml of water was stirred vigorously at room temperature for 5-10 min, after which the dark-cherry-red precipitate of III was removed by filtration, washed with water, and dried.

2-Acetamido-3,4-dimethyl-5-(5-nitro-2-furyl)thiazoline (IV). A solution of 0.2 g (0.84 mmole) of iminothiazoline III in 10 ml of acetic anhydride was refluxed for 0.5 h, after which the mixture was cooled, and the yellow crystals of IV were removed by filtration, washed with water, and air dried.

2-Benzamido-3,4-dimethyl-5-(5-nitro-2-furyl)thiazoline (V). A 0.13-g (0.9 mmole) sample of benzoyl chloride was added to a solution of 0.2 g (0.84 mmole) of iminothiazoline III in 10 ml of pyridine, after which the mixture was heated on a boiling-water bath for 1 h, cooled, and poured into a mixture of 25 g of ice, 25 ml of water, and 10 ml of concentrated HCl. The

TABLE 2. Characteristics of II-V and VII

Compound	mp, °C (from acetic acid)	Found, %			Empirical formula	Calc., %			M^+	Yield, %
		C	H	N (S)		C	H	N (S)		
II	225 (dec.)	31,28	3,42	10,81	$C_{10}H_{12}IN_3O_3S$	31,50	3,15	11,02		82
III	195—197	45,41	3,34	17,87	$C_9H_9N_3O_3S$	45,05	3,77	17,55	239	96
IV	255—257	46,31	3,57	(14,49)	$C_{11}H_{11}N_3O_4S$	46,98	3,91	(14,59	281	83
V	269—271	56,27	3,31	11,87	$C_{16}H_{13}N_3O_4S$	55,98	3,79	12,24	343	69
VII	217—219	46,81	3,66	(14,43)	$C_{11}H_{11}N_3O_4S$	46,98	3,91	(14,59	281	86

precipitate V was removed by filtration and washed with 20 ml of 5% sodium carbonate solution and 10 ml of water.

2-(N-Acetyl-N-methyl)amino-4-methyl-5-(5-nitro-2-furyl)thiazole (VII). A 0.31-g (5.6 mmole) sample of finely ground KOH and 3.7 g (25 mmole) of methyl iodide were added to a solution of 1.5 g (5.6 mmole) of amide VI in 20 ml of DMSO, and the mixture was stirred at room temperature for 20 min. Another 0.31 g (5.6 mmole) of KOH and 3.7 g (25 mmole) of CH_3I were added, and the solution was poured into 50 ml of water after 20 min. The yellow precipitate of VII was removed by filtration, washed with water, and air dried.

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