CYCLIZATION OF 1-ARYLTHIOSEMICARBAZIDES TO BENZOTHIAZOLES

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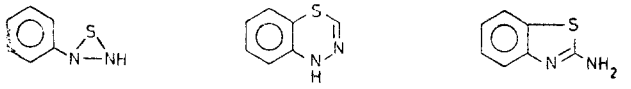
It is known that 1-arylthiosemicarbazides are cyclized to 2-aminobenzothiazoles in acidic media. This reaction was extended to 1,3- and 1,4-disubstituted thiosemicarbazides. It is shown that the rearrangement proceeds through a step involving the formation of o-aminophenylisothioureas. The reaction conditions and substituents in the benzene ring or attached to the nitrogen atoms of the thiosemicarbazides do not have a substantial effect on the ratio of the resulting 2-amino- and 2-phenyl(methyl)aminobenzothiazoles (1:1). In the case of m-chlorophenylthiosemicarbazide, 5- and 7-chloro-2-aminobenzothiazoles are obtained in equimolar amounts, whereas the 7 isomer (5:2) is the major product from m-tolylthiosemicarbazide.

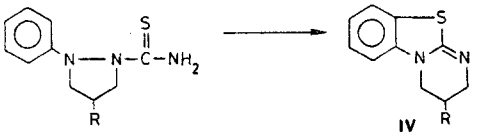
Almost 100 yr ago Fischer [1] observed that 1-phenylthiosemicarbazide reacts with aqueous hydrochloric acid in an ampul at 130°C to give a compound to which he assigned structure I. In 1894 benzothiadiazine structure II was proposed for this product [2]. Nine years later Hugershoff [3] proved that this substance is 2-aminobenzothiazole (IIIa) and expressed the idea that this reaction is related to the Fischer indole synthesis.



I II IIIa

It was recently assumed that the Hugershoff rearrangement proceeds via a scheme involving a sigmatropic shift (for example, see [7]); however, the amount of experimental data on the reaction mechanism and even simply on the effect of substituents on the course of the process is still small.

It was recently shown [4] that the Hugershoff reaction makes it possible to synthesize 2,3,4,5-tetrahydropyrimido[2,1-b]benzothiazoles (IV).



IV

The 4-N atom of the amino group rather than the 2-N hydrazine atom is eliminated during this reaction. However, in the case of a 2-N-unsubstituted thiosemicarbazide the 2-N and 4-N atoms undergo elimination to an equal extent [5], as shown by experiments with labeled nitrogen. The averaging of the isotope content between ammonia and 2-aminobenzothiazole could be a consequence of nucleophilic attack by ammonia on the 2-C atom of the thiazole ring, but special experiments showed that exchange of the amino group does not occur under the selected conditions. This phenomenon is explained by the assumption of the intermediate formation of o-aminophenylisothiourea, especially since similarly constructed compounds that were synthesized by an independent method undergo cyclization to 2-aminobenzothiazoles under the influence of acids [6].

We were able to show that the Hugershoff reaction proceeds poorly in the case of benzene ring substituted compounds if hydrochloric acid is used but proceeds successfully if polyphosphoric acid (PPA) is used [8].

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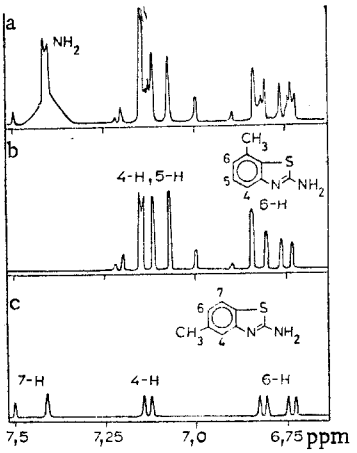
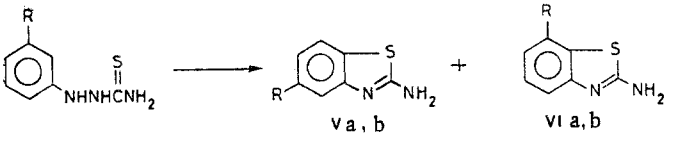


Fig. 1. a) PMR spectrum of the reaction mixture containing 5- and 7-methyl-2-aminobenzothiazoles (in the region of aromatic protons); the spectrum was recorded with decoupling of the protons of the methyl groups; b) theoretical spectrum of 7-methyl 2-aminobenzothiazole (aromatic protons); c) theoretical spectrum of 5-methyl-2-aminobenzothiazole (aromatic protons).

Whereas there was no doubt about the structures of the reaction products in the case of p-substituted 1-phenylthiosemicarbazides, the situation was more complex in the case of the meta isomers. We found that when 1-(m-chlorophenyl)thiosemicarbazide is heated with PPA, it gives a mixture of 5- and 7-chloro-2-aminobenzothiazoles in a ratio of 1:1. For this we recorded the PMR spectra of both individual isomers obtained by an independent method and a mixture of them. It was found that the doublet of the 4-H proton of isomer Va lies at weaker field than the multiplet of 4-H and 5-H protons of VIa. In the spectrum of a mixture of the isomers the ratio of the integral intensities of these signals is 1:2, i.e., there is one 4-H proton of isomer VIa per 4-H proton of benzothiazole Va.



Va, b VI a,b

V, VI a R=Cl, b R=CH3

When 1-(m-tolyl)thiosemicarbazide is heated with PPA, it gives a mixture of substances, from which homogeneous [according to thin-layer chromatography (TLC); no separation can be achieved by crystallization] crystals can be obtained by one crystallization from water (m-toluidine and impurities with unknown structures are separated). According to the PMR spectrum, the mixture consists of 5- and 7-methyl-2-aminobenzothiazoles in a ratio of 2:5 (the same ratio as in the reaction mixture), which follows from a comparison of the integral intensities of the signals of the methyl groups. For the unambiguous assignment of the signals of the aromatic protons we used a theoretical calculation of the spectra of both isomers by means of the Varian Spin Simulation program with a Varian 620/1 computer. The signals of the aromatic protons of each isomer constitute a three-spin system (of the ABC type); in addition, spin–spin coupling between the protons of the CH_3 group in the 5 or 7 position and the protons of the benzene ring is observed. Thus the signals of the aromatic protons comprise the ABC part of an $ABCX_3$ system, where X_3 are the protons of the methyl group. The experimental spectrum was obtained under conditions involving the suppression of the spin–spin coupling of the methyl protons with the aromatic protons (for simplification of the ABC portion of the spectrum).

We used the spin–spin coupling constants (SSCC) and the chemical shifts for 2-methylbenzothiazoles presented in [9], the authors of which made a complete analysis of the proton spectrum of this compound, as the initial approximation for the calculations. The SSCC and chemical shifts were then varied until they were in the best agreement with the experimental and theoretical spectra (see Fig. 1). We were thus enabled to assign the lines in the spectra

TABLE 1. PMR Spectra of 2-Aminobenzothiazoles*

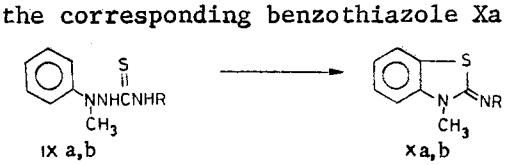
Compound	Substituent	δ, ppm						SSCC, J, Hz					
		CH_3	4-H	5-H	6-H	7-H	NH_2	J_{45}	J_{56}	J_{67}	J_{46}	J_{57}	J_{47}
Vb	5-CH_3	2,28	(7,14)[b]	—	(6,80)	7,47	7,35—7,47	—	—	(8,0)	(1,6)	—	(0,3)
IIIb	6-CH_3	2,26	7,20	6,98	—	7,41	7,28	8,2	—	—	—	1,7	0,2
VIb	7-CH_3	2,30	(7,16)	(7,08)	(6,80)	—	7,35—7,47	(8,3)	(7,5)	—	(1,7)	—	—
Vc	5-Cl	—	7,37	—	7,00	7,61	7,67	—	—	8,2	2,2	—	
IIIc	6-Cl	—	(7,27)	(7,18)	—	7,72	7,55	(8,5)	—	—	—	(2,2)	(0,4)
VIa	7-Cl	—	(7,28)	(7,22)	(7,06)	—	7,71	(8,0)	(7,3)	—	(1,5)	—	—
VII	5-CH_3O	3,71	6,92	—	6,60	7,45	7,40	—	—	8,6	2,5	—	0,3
VIII	6-CH_3O	3,69	(7,23)	(6,79)	—	(7,25)	7,21	(8,8)	—	—	—	(2,6)	(0,3)

*The spectra of the compounds in d_6-DMSO were recorded with a Varian XL-100-15 spectrometer with hexamethyldisiloxane as the internal standard. b) The calculated δ values and SSCC are presented in parentheses. c) The spectrum was recorded with a Varian T-60 spectrometer.

of each isomer and thoroughly analyze the PMR spectrum of the mixture of isomers, from which it follows that we are dealing with a mixture of only two substances with clear predominance of the 7 isomer (VIb). The more intense signal of the methyl group at 2.30 ppm consequently corresponds to the 7-CH_3 group. The signal at stronger field corresponds to the methyl group in the 5 position. It is interesting that the signal of the methyl group of 6-methyl-2-aminobenzothiazole appears at 2.26 ppm. The chemical shifts and the SSCC of these three isomers and of 5-chloro- (Va), 6-chloro- (IIIc), 7-chloro- (VIa), 5-methoxy- (VII), and 6-methoxy-2-aminobenzothiazoles (VIII) are presented in Table 1.

It should be emphasized that the signals of both the aromatic protons and the methyl groups in the ortho position relative to the sulfur atom are the weakest-field signals. The signals of the proton or CH_3 group in the 4 position are found at stronger field, followed by the signals of the proton or CH_3 group in the 5 position. The signals of the substituent in the 6 position are found at strongest field. This is in agreement with the data in [9] on the spectra of 2-methylbenzothiazoles. Replacement of the methyl group in the 2-position of the benzothiazole by an amino group consequently leads to a weak-field shift of approximately the same magnitude (~0.5 ppm) of all of the signals of the aromatic protons. Paris and co-workers [10] have described the PMR spectrum of 6-methyl-2-morpholinomethylaminobenzothiazole. The 5-H chemical shifts and SSCC of the aromatic protons virtually coincide with our data for 6-methyl-2-aminobenzothiazole (IIIb).

If there is a methyl group (IXa) attached to the 1-N atom in the 1-phenylthiosemicarbazide molecule, the yield of the corresponding benzothiazole Xa decreases somewhat.



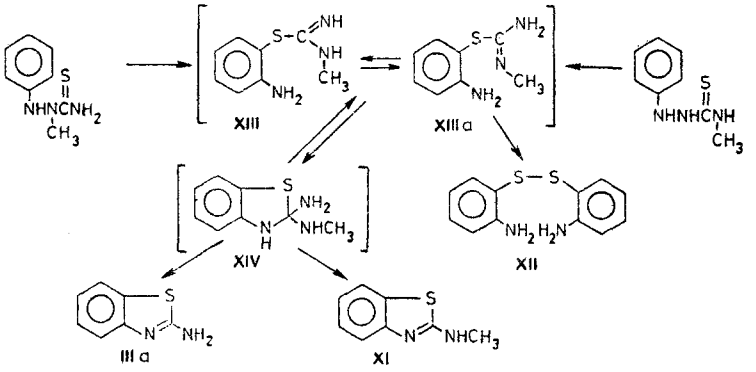
IX a,b — Xa,b

IX, X a R=H, b R=C_6H_5

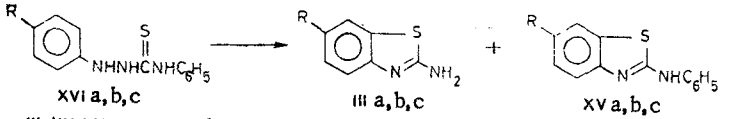
However, in the case of 2- or 4-methyl-1-phenylthiosemicarbazides, in addition to the expected benzothiazoles IIIa and XI, 2,2'-diaminodiphenyl sulfide XII can be isolated in some cases in 25-26% yields. Sulfide XII is formed during strong alkalization of the reaction mixture in the process of decomposition of the PPA, evidently as a result of hydrolysis of the uncyclized isothiourea XIII. This reaction is well known for isothioureas and even serves as a preparative method for the synthesis of mercaptans [11]. The resulting o-aminothiophenol is readily oxidized to the disulfide [12]. We demonstrated by special experiments that benzothiazoles IIIa or XI are not hydrolyzed under these conditions. The formation of disulfide XII consequently may serve as proof for reaction through a step involving the isothiourea (or more precisely its protonated form).

2-Methyl- and 4-methyl-1-phenylthiosemicarbazides are of interest in that they should have the same intermediate XIV and the ratios of the resulting benzothiazoles should consequently be identical. In fact, it was shown by liquid chromatography that the resulting reaction mixtures are identical. Moreover, benzothiazoles IIIa and XI are formed in equi-

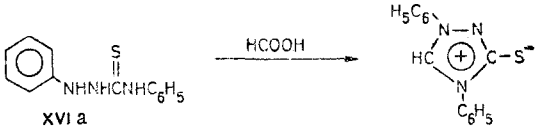
molar amounts in both cases. The cleavage of the bonds in the intermediate consequently does not depend substantially on the presence of a methyl group attached to the nitrogen atom.



It was found that in the case of models with a phenyl group attached to the 4-N atom the probabilities of cleavage of the C—NH and C—NPh bonds are virtually equal; substituents (chloro and methyl) in the benzene ring of 1-aryl-4-phenylthiosemicarbazide have almost no effect on the ratio of the resulting benzothiazoles III and XV (according to TLC data).



A complex mixture is obtained when 1,4-diphenylthiosemicarbazide (XVIa) is heated in glacial acetic acid or trifluoroacetic acid. However, the mesoionic 1,4-diphenyl-1,2,4-triazoline-3-thione is formed in the case of 85% hydrochloric acid; this is in agreement with the literature data [13].



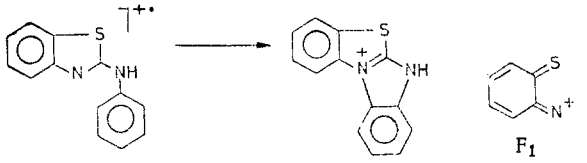
As in the case of 1-arylthiosemicarbazides, KU-2 resin in the H^+ form (at room temperature in alcohol) does not give rise to any changes in thiosemicarbazide XVIa. 2-Phenylaminobenzothiazole (XVa) and small amounts of decomposition products are formed when 1,4-diphenylthiosemicarbazide is heated without a catalyst or a solvent above its melting point. 2-Aminobenzothiazole (IIIa) cannot be detected, since it is thermally unstable and decomposes under these conditions (this was confirmed by special experiments). Primarily amines IIIa and XVa in a ratio of 1:1 are formed in PPA at 120, 180, and 205°C. Amines IIIa and XVa are formed in the same (1:1) ratio (according to TLC) in orthophosphoric acid at 120°C, in concentrated hydrochloric acid at 120°C (sealed ampul), and in 33% alcoholic HCl (sealed ampul on a water bath).

However, in the case of the reaction of 1-methyl-1,4-diphenylthiosemicarbazide (IXb) in PPA at 120°C substituted imine Xb was isolated from the reaction mixture in 44% yield. However, the PMR spectrum of the reaction mixture (in trifluoroacetic acid) contains two singlets of aliphatic protons at 3.80 and 3.65 ppm in a ratio of 5:1; on the basis of a comparison with the spectra of the individual compounds, these singlets were ascribed to the signals of the CH_3 groups of, respectively, Xb and Xa (the methyl group in Xb falls into the region of anisotropy of the benzene ring of the phenylimino group). Thus if the mixture contains imine Xa, cleavage of the C—N bond in which the nitrogen atom is not bonded to the aromatic ring is the primary process in the formation of the thiazolidine ring.

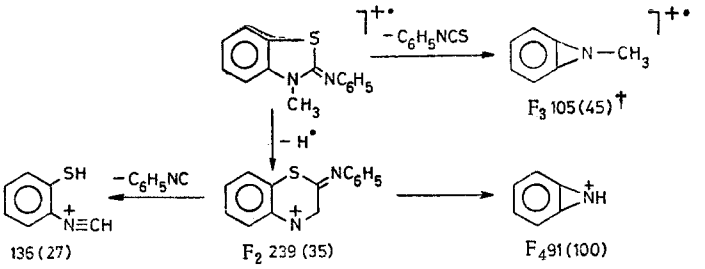
The UV spectra of 2-phenylaminobenzothiazoles* contain two intense (log ε 4.5) absorption bands at 220 and 300 nm. The introduction of substituents such as chloro or methyl does not change the spectral pattern substantially. The long-wave maximum is more intense than in the case of 2-aminobenzothiazoles.

*The UV and mass spectra of 2-aminobenzothiazoles were described in [8].

2-Phenylaminobenzothiazoles XV are characterized by high stability with respect to electron impact (W_M = 20-38%). The molecular ion peak is the maximum peak in the spectra of these compounds. The principal pathway in the fragmentation of XV is elimination of a hydrogen atom, which is evidently split out from the phenyl group, as in [14], with the simultaneous formation of a C—N bond:



The $[M - H]^+$ ion is also extremely stable. The molecular ion and $[M - H]^+$ ion account for 34-62% of the total ion current. The spectra of XVb and XVc also contain a low-intensity ion at 225,* the formation of which is associated with the elimination of the substituent from the 6 position of the benzothiazole. In addition, the successive elimination of two hydrogen atoms from the molecular ion is also characteristic for benzothiazole XVb. If the loss of one hydrogen atom is a common pathway in the fragmentation of the molecular ions of 2-phenylaminobenzothiazoles, the elimination of yet another hydrogen atom can be linked to the presence of a CH_3 group. The process then is a rearrangement process, i.e., a hydrogen atom is split out from the methyl group with expansion of the benzene ring [15]. The spectra of all of the investigated XV contain a low-intensity peak of ions at 122, which probably have the F_1 structure and are formed as a result of elimination of a PhNC molecule from the $[M - R]^+$ ions. This process is similar to the elimination of HCN from the molecular ion of 2-aminobenzothiazoles [8], but it is manifested more weakly in this case.



The introduction of a substituent in the 3 position of 2-phenylaminobenzothiazole (Xb) sharply reduces the stability of the molecule with respect to electron impact. The elimination of hydrogen becomes less characteristic and proceeds via a different mechanism involving expansion of the thiazole ring (the F_3 ion). This is characteristic for N-methyl-substituted five-membered heterocycles [16]. The elimination of a molecule of phenyl isothiocyanate leads to a rather intense F_3 ion. The most intense ion in the spectrum of Xb is the ion at 91, which evidently has the F_4 structure. As in the case of the F_2 ion, a rearrangement process is assumed to be responsible for its formation.

EXPERIMENTAL

The UV spectra of alcohol solutions of the compounds were recorded with Cary and Specord spectrophotometers. The IR spectra of mineral oil suspensions of the compounds were recorded with IKS-22 and UR-20 spectrometers. The mass spectra were recorded with an MKh-1303 spectrometer with introduction of the samples directly into the ion source at an ionizing-electron energy of 50 eV. The PMR spectra were recorded with a Varian T-60 spectrometer. Chromatographic analysis was performed by Yu. M. Sapozhnikov with a Spectra-Physics 3500 B liquid chromatograph. The stainless-steel column was 0.5-m long and had an internal diameter of 2.1 mm; it was filled with Merck silanized silica gel (30 μ). Elution was accomplished with 18% aqueous ethanol at a feed rate of 0.47 ml/min, a pressure of 150 atm, and an analysis temperature of 50°C. The apparatus had a UV detector (254 nm). The recording ribbon rate was 10 cm/h, and the sample volume was 10 μl.

The reaction mixtures containing benzothiazoles III and XV were investigated with an Opton PMQ II scanning spectrophotometer for chromatography. The reference samples and arti-

*Here and subsequently, the m/e values are presented for the ion peaks.
†The percentage of the maximum ion peak is given in parentheses.

ficial and reaction mixtures were applied to a Silufol UV-254 plate and chromatographed. The chromatographic zones were recorded by measurement of the absorption of UV emission at 254 nm by the substances. The measurements were made as the chromatogram was moved in a direction coinciding with the direction of chromatography relative to a rectangular probe (7 by 0.5 mm). A calibration graph of the dependence of the ratio of the areas of five benzothiazoles on the composition of artificial mixture was constructed for quantitative estimates.

Differential thermal analysis (DTA) of 1,4-diphenylthiosemicarbazide and 2-amino- and 2-phenylaminobenzothiazoles was carried out with a Perkin–Elmer DSC-1B differential scanning calorimeter at 30-300°C and showed that 2-aminobenzothiazole melts at 130°C and begins to decompose at 146°C, 2-phenylaminobenzothiazole melts at 163°C and does not decompose at up to 300°C, and 1,4-diphenylthiosemicarbazide begins to decompose as it melts (190°C).

The preparation of thiosemicarbazides and benzothiazoles IIIa-c, Va, VIa, VII, and VIII was described in [8, 17].

3-Methyl-2-iminobenzothiazole. This compound, with mp 122-123°C (from water) [18], was obtained in 51% yield by the action of PPA on 1-methyl-1-phenylthiosemicarbazide by the method in [8]. IR spectrum: 3245 cm^{-1}. UV spectrum, λ_{max} (log ε): 222 (4.57), 261 (4.03), and 295 nm (3.77). PMR spectrum (in CF_3COOH with hexamethyldisiloxane as the external standard): 3.67 (3H, s, CH_3) and 7.3-7.9 ppm (4H, m, aromatic protons). Mass spectrum: $[M]^+$ 164 (100), 163 (5), 149 (1), 137 (6), 136 (87), 122 (20), 121 (5), 109 (6), 96 (4), 82 (6), 78 (6), 69 (6), 63 (3).

2-Methylaminobenzothiazole. A 4.3-ml (0.048 mole) sample of aniline was added to a solution of 3.48 g (0.048 mole) of methyl isothiocyanate in 20 ml of chloroform, and the mixture was heated on a water bath for 2 h. It was then cooled to room temperature, and a solution of 2.6 ml (0.05 mole) of bromine in 20 ml of chloroform was added dropwise with stirring. The mixture was then allowed to stand overnight, and the resulting light-colored precipitate was removed by filtration and suspended in 100 ml of water. A stream of SO_2 was passed through the suspension until the solid dissolved completely, after which the mixture was made alkaline with solid KOH, and the white precipitate was removed by filtration to give 5.2 g (68%) of 2-methylaminobenzothiazole with mp 136-137°C (from aqueous alcohol). UV spectrum, λ_{max} (log ε): 222 (4.50), 265 (4.14), and 289 sh nm (3.50). PMR spectrum (in CF_3COOH with tetramethylsilane as the internal standard): 3.35 (3H, d, J = 4.5 Hz, CH_3), 7.33-7.97 ppm (4H, m, aromatic protons), and 8.33 (1H, d, NH). According to the data in [19], this compound has mp 138°C.

Cyclization of the Thiosemicarbazides

In accordance with the general method in [8], 570 mg (3.1 mmole) of 1-(m-tolyl)thiosemicarbazide was treated with PPA, and the mixture was worked up to give 350 mg of a mixture with mp 144-150°C. Recrystallization from water to give a product with mp 149-160°C. The mixtures before and after crystallization were investigated by PMR spectroscopy with a Varian XL-100-15 spectrometer (100.1 MHz) in deuterodimethyl sulfoxide with hexamethyldisiloxane as the internal standard.

A 700-mg (3.5 mmole) sample of 1-(m-chlorophenyl)thiosemicarbazide was similarly treated with PPA, and the mixture was worked up to give 490 mg of a mixture with mp 125-150°C, which was investigated as in the preceding experiment.

4-Methyl-1-phenylthiosemicarbazide (70 mg) was heated with 2 ml of PPA at 120°C for 6 h, after which the mixture was poured over ice, and the aqueous mixture was made alkaline with solid KOH with cooling under ether to pH 10-11. It was then extracted with 150 ml of ether and 50 ml of chloroform, and the extract was dried with Na_2SO_4. The solvent was removed by evaporation, and the residual mixture was investigated with a liquid chromatograph. The compounds had the following retention times: 2-aminobenzothiazole IIIa 12 min and 7 sec, 2-methylaminobenzothiazole XI 19 min and 45 sec, and 2,2'-diaminodiphenyl disulfide XII 60 min.

2-Methyl-1-phenylthiosemicarbazide was treated with PPA under similar conditions. The liquid chromatogram of the reaction mixture was identical to the chromatogram of the preceding experiment.

A 950-mg (5.2 mmole) sample of 4-methyl-1-phenylthiosemicarbazide was heated with PPA at 120°C for 6 h, after which the mixture was worked up as above. The reaction mixture (440 mg) was separated preparatively in a thin layer of aluminum oxide in a benzene–ethyl acetate

system (3:1). The fraction with R_f 0.6-0.8 was collected and worked up to give 165 mg (25%) of yellow crystals of 2,2'-diaminodiphenyl disulfide XII with mp 89°C (from absolute alcohol). UV spectrum, λ_{max} (log ε): 222 (4.65) and 340 nm (4.05). PMR spectrum (in $CDCl_3$ with hexamethyldisiloxane as the internal standard): 3.7-4.3 (4H, s, NH_2), and 6.3-7.3 ppm (8H, m, aromatic protons). Mass spectrum:* $[M]^+$ 248 (23), 126 (10), 125 (89), 124 (100), 97 (21), 93 (28), 81 (18), 80 (67), 69 (18), 65 (13), 63 (11). IR spectrum: 3319 and 3390 cm^{-1}. According to the data in [20], this compound has mp 88°C.

As in the preceding case, 170 mg (26%) of XII was obtained from 2-methyl-1-phenylthiosemicarbazide after preparative separation in a thin layer of aluminum oxide in the same system. The product was recrystallized successively from aqueous alcohol and hexane to give a substance with mp 89°C. No melting-point depression was observed for a mixture of this product with a sample obtained from 4-methyl-1-phenylthiosemicarbazide. The IR spectra of the two samples were also identical.

The cyclization of 1,4-diarylthiosemicarbazides IXb and XVI was carried out in PPA by the method in [8] at 120°C. For the cyclization of the corresponding benzothiazoles, the residue after evaporation of the solvent was separated with a column (15 by 200 mm) with L 100/160 silica gel by successive elution of benzothiazoles XV (Xb) and III by elution with chloroform. In the preparation of IIIa and XVa the reaction mixture after removal of the solvent by evaporation was crystallized from water (2-aminobenzothiazole IIIa was obtained); the residue was recrystallized from benzene (2-phenylaminobenzothiazole XVa was obtained). Compounds IIIa-c and XVa, which were isolated in 16, 14, 42, and 21% yield, respectively, were identified by comparison with the benzothiazoles obtained by alternative synthesis [8, 21]. The physical constants of XV and Xb are presented in Table 2.

Cyclization of 1,4-Diphenylthiosemicarbazide XVIa under Other Conditions. A) A 100-mg (0.4 mmole) sample of XVa was heated with PPA at 180°C for 5 h, after which the mixture was worked up in the usual way [8], and the mixture of products was investigated with an Opton PMQ II spectrometer for chromatography.

B) The reaction was carried out at 205° for 1 h, after which the mixture was worked up and the mixture of products was investigated similarly.

C) A 100-mg (0.4 mmole) sample of thiosemicarbazide XVIa was heated with 2.5 ml of orthophosphoric acid at 120° for 5 h, after which the mixture was cooled and diluted with water, and the aqueous mixture was made alkaline to pH 10 and extracted with ether. The extract was dried with K_2CO_3, the ether was removed by evaporation, and the mixture of products was investigated similarly.

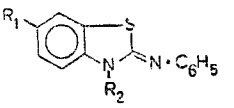
D) A 100-mg (0.4 mmole) sample of thiosemicarbazide XVI was heated in a sealed ampul with 5 ml of concentrated hydrochloric acid at 120°C for 12 h, after which the mixture was diluted with water and made alkaline to pH 10 with sodium carbonate. The resulting precipitate, which was a mixture of benzothiazoles IIIa and XVa, was removed by filtration and investigated as in the preceding experiments.

E) A 120-mg (0.5 mmole) sample of thiosemicarbazide XVIa was heated in a sealed ampul with 4 ml of 33% alcoholic HCl solution for 8 h on a water bath, after which the alcohol was removed by evaporation, water was added to the residue, and the aqueous mixture was made alkaline and extracted with ether. The extract was dried with K_2CO_3, and the ether was removed by evaporation. The residual mixture was investigated as in the preceding experiments. In experiments A-E the IIIa:XVa ratio was close to 1:1.

A 200-mg (0.82 mmole) sample of thiosemicarbazide XVIa was heated at 230°C for 30 min, after which the material was cooled and separated preparatively in a thin layer of aluminum oxide in a benzene–methanol system (10:1). The fraction with R_f 0.28-0.64 was collected, and the solvent was removed by evaporation to give 20 mg of chromatographically pure 2-phenylaminobenzothiazole XVa, which did not depress the melting point of an authentic sample. Mass spectrum: $[M]^+$ 226.

1,4-Diphenyl-1,2,4-triazoline-3-thione. A 200-mg (0.82 mmole) sample of thiosemicarbazide XVIa was heated with 5 ml of 85% hydrochloric acid at 110°C for 20 h, after which the mixture was diluted with water, and the aqueous mixture was made alkaline to pH 10 with NaOH

*The spectrum was recorded with a DS-50 spectrometer with introduction of the samples directly into the ion source at an ionizing-electron energy of 70 eV at 190°C.

TABLE 2. 2-Phenylaminobenzothiazoles 

Compound	R_1	R_2	mp, °C (lit. mp)	PMR spectrum, δ, ppm	UV spectrum, λ_{max}, nm (log ε)	Mass spectrum, m/e (percent of the maximum)	Yield, %
XVa	H	H	163 (157)[21]		218—220 (4,30), 236 (4,23), 300—302 (4,36)	226 (98), 225 (98), 195 (9,8), 119 (16), 113 (7), 96 (11), 91 (25), 81 (14), 77 (43), 69 (40), 57 (23).	21
XVb	CH_3	H	163—164 (164)[22]	2,27 (3H, s CH_3), 6,80—7,80 (9H, m aromatic and NH protons)[b]	222 (4,55), 233 sh (4,50), 292 sh (4,62), 298 (4,43), 304 sh (4,62)	240 (100), 239 (76), 238 (8), 136 (7), 122 (3), 121 (6), 120 (5), 119 (8), 110 (7), 109 (4), 78 (6), 77 (23), 69 (4), 66 (3), 65 (6), 63 (3)	26
XVc	Cl	H	198—200 (192)[22]		221 (4,26), 240 (4,25), 306 (4,41)	262 (29), 261 (34), 260 (100), 259 (77), 130 (26), 122 (15), 112 (10), 107 (7), 96 (6), 95 (12), 91 (5), 82 (6), 81 (5), 79 (7), 78 (8), 77 (85), 76 (10), 75 (7), 73 (5), 69 (30), 65 (28), 64 (10), 63 (51)	35
Xb	H	CH_3	97—98 (96)[23]	3,80 (3H, s CH_3), 7,10—7,50 (9H, m aromatic protons)[b]	223 (4,64), 302 (4,21)	240 (64), 239 (35), 136 (27), 109 (12), 106 (18), 105 (45), 95 (10), 91 (100), 83 (12), 81 (22), 77 (20), 73 (10), 71 (17), 70 (10), 69 (58), 57 (36)	44

*a) The spectrum in deuterodimethyl sulfoxide was recorded with hexamethyldisiloxane as the internal standard. b) The spectrum in CF_3COOH was recorded with hexamethyldisiloxane as the external standard.

solution. The resulting precipitate (190 mg) was washed on the filter with water and recrystallized from water to give 100 mg of 1,4-diphenyl-1,2,4-triazoline-3-thione with mp 214-215°C. UV spectrum, λ_{max} (log ε): 243-245 (4.32) and 316 nm (3.18). Mass spectrum: $[M]^+$ 253 (7), 252 (8), 135 (50), 118 (15), 104 (14), 93 (40), 91 (43), 77 (100), 76 (9), 66 (8), 65 (10), 63 (7). According to the data in [13], this compound has mp 216-217°C. UV spectrum, λ_{max} (log ε): 244 (4.32) and 324 nm (3.52).

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DAKIN–WEST REACTION IN THE 2-IMINO-3-THIAZOLINYLACETIC ACID SERIES

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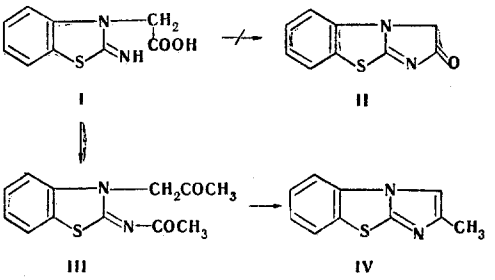
The reaction of 2-imino-3-benzothiazolinylacetic acid with acetic anhydride under the conditions of the Dakin–West reaction leads to 3-acetonyl-2-acetimidobenzothiazoline. Under the same conditions 2-imino-3-thiazolinylacetic acid gives 5-acetyl-6-hydroxyimidazo[2,1-b]thiazole. The structures of the compounds obtained were proved by means of their IR, PMR, and mass spectra.

It is known that the corresponding acylamino ketones (the Dakin–West reaction) [1] are formed in the reaction of various α-amino acids, including heterocyclic α-nitrogen-containing acids such as 1-uracilylacetic or 3-methyl-6-pyridazinonylacetic, with acetic anhydride in pyridine. In addition, it has been reported [2] that under similar conditions 2-imino-3-benzothiazolinylacetic acid (I) is converted to benzothiazolo[3,2-a]imidazol-2-one (II), whereas 2-imino-3-thiazolinylacetic acid reacts with acetic anhydride in benzene to give 5,6-dihydro-5,5-diacetylimidazo[2,1-b]thiazol-6-one [3]. It seemed of interest to ascertain the reasons for the unusual Dakin–West reaction in these cases.

In the reaction of 2-imino-3-benzothiazolinylacetic acid with acetic anhydride in pyridine under the conditions of the Dakin–West reaction [1] we obtained the expected product of this reaction — 3-acetonyl-2-acetimidobenzothiazoline (III), the conversion of which to the described benzothiazole IV [2, 4] proves its structure. The scheme of the transformations realized in this case is evidently similar to the Dakin–West reaction for N,N-disubstituted α-amino acids that are incapable of forming derivatives of the oxazole series [1].



I II III IV

We did not observe the formation of the previously described [2] II in this case.

Distinct singlets of the protons of acetyl groupings at 2.11 and 2.23 ppm, a singlet at 5.79 ppm, which we assigned to the resonance of the protons of the N-methylene grouping, and a complex multiplet of aromatic protons at 7.09-7.90 ppm are observed in the PMR spectrum of III. The ratio (3:3:2:4) of the integral intensities of the signals confirms our assignment.

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