mole) of tert-butylamine, and 14.4 ml (∿0.18 mole) of formalin was stirred at room temperature for 30 min, after which the mixture was extracted with benzene (three 20-ml portions). The benzene extract was dried with sodium sulfate, the benzene was removed by distillation, and IIi was precipitated from the residue by means of hexane. PMR spectrum: ∿4.79 (1H, m, 6'-CH_2); 4.79 (2H, s, 2-CH_3); 4.52 (2H, s, 4-CH_2); ∿3.96 (1H, m, 6'-CH_2); 3.96 (2H, s, 2'-CH_2); 3.02, 3.13, 3.20, 3.31 (2H, 4'-CH_2); 1.18 (9H, s, tert-Bu); 1.08 ppm (9H, s, tert-Bu).

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PRODUCTS OF TRANSFORMATION OF ALDEHYDE BENZAZOLYLHYDRAZONES IN ACETIC ACID IN THE PRESENCE OF n-AMYL NITRITE

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The reaction of aldehyde benzazolylhydrazones with amyl nitrite in acetic acid leads to an oxidative transformation to give N,N'-diacyl derivatives of 2-hydrazinobenzazoles rather than to nitrosation of the hydrazones, whereas in the case of benzaldehyde benzothiazolylhydrazone it leads to 1,4-dibenzothiazolyl-3,6-diphenyl-1,4-dihydro-1,2,4,5-tetrazine.

The nitrosation of aldehyde benzothiazolyl- and benzimidazolylhydrazones with n-amyl nitrite in alkaline and neutral media leads to the formation of the corresponding azo ketoximes [1]. However, some hydrazones, such as benzaldehyde benzothiazolylhydrazone, cannot be subjected to reaction under these conditions. At the same time, it is known that under the influence of a nitrosating agent in acetic acid arylhydrazones give nitroso products, which undergo isomerization to arylazo ketoximes [2].

In this connection, we investigated the reaction of benzazolylhydrazones I-III (see the scheme) with amyl nitrite in acetic acid. Instead of the expected oximes, we obtained compounds, the formation of which can be explained by transformations with the participation of n-amyl nitrite as an oxidizing agent rather than as a nitrosating agent. It is known [3, 4] that the oxidation of monosubstituted hydrazones proceeds in extremely diverse ways. Depending on the electronic properties of the substituent in the hydrazone molecule and the nature of the oxidizing agent and the solvent, the following products may be obtained: azo hydroxyperoxides, azo acetates, azo olefins, and dimeric compounds and products of their subsequent transformation, viz., substituted 1,2,4-triazoles, tetrazines, etc.

Compounds I-III were subjected to reaction with amyl nitrite at room temperature or with brief heating (3-5 min) using a twofold excess of freshly prepared n-amyl nitrite. Chromatographic analysis [by thin-layer chromatography (TLC)] of the reaction mixture showed

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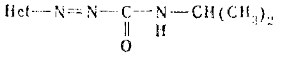
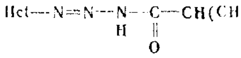
that several substances were formed in the reaction. Compounds IV-VI were isolated by column chromatography. According to the IR-spectral data, they contained NH and CO groups. One might have assumed two variants. In the first variant nitrosation of the benzazolylhydrazones leads to the formation of the corresponding oximes, which undergo the Beckmann rearrangement to amides in acidic media. In this case in the nitrosation of, for example, isobutyraldehyde benzothiazolylhydrazone (I) one should have expected the production of one of two amides A or B (with allowance for the stereospecificity of the rearrangement) with empirical formula $C_{11}H_{12}N_4OS$:



$$Het-N=N-\underset{\displaystyle O}{\underset{\|}{C}}-\underset{H}{N}-CH(CH_3)_2$$

A

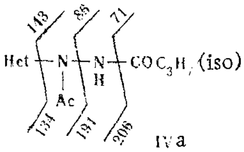


$$Het-N=N-\underset{H}{N}-\underset{\displaystyle O}{\underset{\|}{C}}-CH(CH_3)_2$$

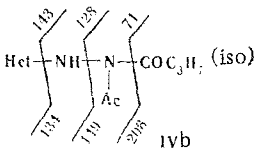
B

In addition, amyl nitrite may act as an oxidizing agent, and in acetic acid one might expect the formation of N-acyl-N'-acetylbenzothiazolylhydrazine IV, which has empirical formula $C_{13}H_{15}N_3O_2S$ (see the Scheme).

According to the results of high-resolution mass spectrometry, the compound that we obtained in the reaction of hydrazone I with amyl nitrite in acetic acid has a mass corresponding to empirical formula IV. The elimination of one molecule of ketene from M^+ (see the experimental section) indicates that there is a second carbonyl group in the isolated compound. The N-isobutyryl-N'-acetylbenzothiazolylhydrazine structure IVa or IVb can be assigned to the compound obtained:



IVa



IVb

The data from the IR and PMR spectra do not make it possible to choose between these structures.

It is known [6, 7] that hydrazines are readily cleaved at the N–N bond under the influence of electron impact. In this case when the reaction pathway that leads to structure IVa is realized, ions* at 191 and 86 (or, the case of possible migration of hydrogen from the isopropyl grouping to the site of cleavage, ions at 192 and 85) should be recorded in the mass spectrum, whereas ions at 149 and 128, respectively, should be recorded in the case of the formation of structure IVb. The mass spectrum obtained is characterized by ions at 192 and 85. The ion recorded at 149 arises due to elimination of an acetyl group from the ion at 192 with the $[Het - \overset{+}{N}COCH_3]$ structure.

Thus the mass-spectrometric data and the literature data [8] indicate the formation of the IVa structure.

The reaction proceeds similarly with hydrazone III. N-Benzoyl-N'-acetyl-N'-(1-benzyl-2-benzimidazolyl)hydrazine (VI) was isolated from the reaction mass.

However, reaction products V and VII were isolated in quite high yields in the case of benzaldehyde benzothiazolylhydrazone (II). The IR spectrum of V contains absorption bands of NH and CO groups. The molecular ion is characterized by cleavage of the amide bond and the appearance in the mass spectra of an intense peak of an ion that corresponds to a benzoyl cation structure and a peak of an ion that corresponds to a benzothiazolylhydrazine cation fragment (see the experimental section). Thus V is N-benzoyl-N'-benzothiazolylhydrazine. The V structure was confirmed by alternative synthesis.

The characteristic bands of NH and CO stretching vibrations are not observed in the IR spectrum of VII. It contains only stretching (skeletal) vibrations of a benzothiazole ring (C=O, 1605 and 1575 cm^{-1}) and out-of-plane deformation vibrations of ring CH bonds at 728, 750, and 762 cm^{-1}. Only signals of aromatic protons, which give a complex multiplet at 7.0-8.3 ppm, are observed in the PMR spectrum of a solution in d_6-DMSO. The electronic spectrum of VII virtually coincides with the spectrum of the starting hydrazone [λ_{max} = 220 and 330 nm (ethanol) for benzaldehyde benzothiazolylhydrazone II and λ_{max} = 215 and 335 nm for VII]. Fragmentation of the molecular ion is characterized by the appearance of an intense ion peak at 251 (see the experimental section), which constitutes evidence for the symmetrical struc-

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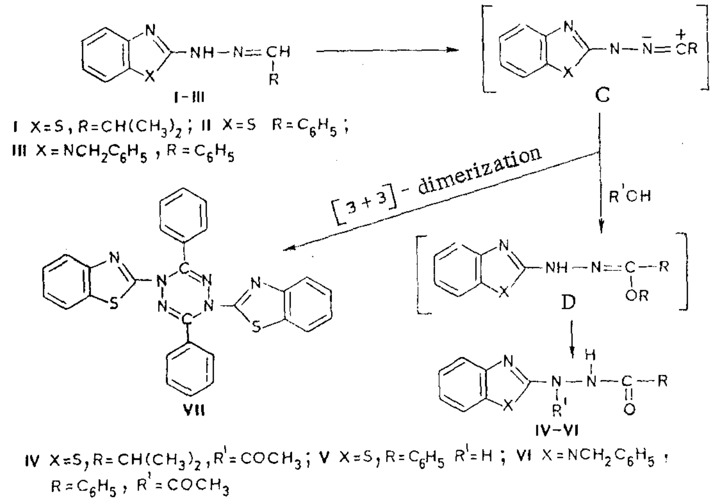
*Here and subsequently, the m/z values are given for the ion peaks.

ture of M^{+} and its cleavage to give two ions with identical masses. The presence in the mass spectrum of fragment ions at 92, 108, 122, 123, 134, and 148 is due to a fragment with the [Het — $\overset{+}{N}$] structure. In addition, the peak of an ion corresponding to $[M - (Het) - N]^{+}$ is recorded (see the experimental section). The ion peak at 77 indicates the presence of a phenyl group, while the ion peak at 103, which has a benzonitrile cation structure, proves the orientation of the phenyl substituent in the compound. The interpretation of the principal fragment ions and the data from IR, PMR, and electronic spectroscopy constitute evidence that VII corresponds to the 1,4-dibenzothiazolyl-3,6-diphenyl-1,4-dihydro-1,2,4,5-tetrazine structure (see the scheme) and is the product of oxidative dimerization of the starting hydrazone. Unfortunately, we were unable to obtain the ^{13}C NMR spectrum of VII because of its insufficient solubility in acetone, chloroform, and dimethyl sulfoxide.

The mechanism of the formation of IV-VII was not investigated; however, on the basis of the literature data, it may be assumed that the transformation proceeds through the formation of nitrilimines. It is known [9] that aryl- and hetarylhydrazones can generate nitrilimines under the influence of lead tetraacetate. It is apparent that the action of n-amyl nitrite on benzazolylhydrazones I-III also generates nitrilimines (B), which readily undergo [3 + 3] dimerization to give tetrazines and also under 1,3-addition. The hydrazones (D) that are formed in the reaction of the nitrilimines with acetic acid (or water) undergo migrational rearrangement to disubstituted hydrazines IV-VI as in [8].

Scheme



Thus for the first time we have established the possibility of the one-step preparation from hetarylhydrazones of compounds such as diacylheterylhydrazines and tetrasubstituted dihydrotetrazines that are difficult to obtain by other methods. The resulting derivatives of the benzazole series may be of interest as potential biologically active substances.

EXPERIMENTAL

The IR spectra of the compounds were recorded with a UR-20 spectrometer. The PMR spectra were recorded with a Perkin-Elmer R-12B spectrometer (60 MHz) with tetramethylsilane as the internal standard. The mass spectra were recorded with a Varian MAT-311A spectrometer with direct introduction of the samples; the accelerating voltage was 3 kV, the emission current was 300 μA, the ionizing-electron energy was 70 eV, and the vaporization temperature of the samples ranged from 80 to 250°C. The high-resolution mass spectra were obtained under the same conditions: $M/\Delta M$ 15000, and the standard was polyphosphoric acid. The compositions of the reaction mixtures and the purity of the substances were monitored by TLC on Silufol UV-254 plates in chloroform and ethyl acetate. The substances were purified by chromatography of the mixtures with a column packed with silica gel (40/100 μ) by elution with chloroform.

N-Isobutyryl-N'-acetyl-N'-benzothiazolylhydrazine (IV). A 2 ml (20 mmole) sample of n-amyl nitrite was added to a solution of 2 g (10 mmole) of isobutyraldehyde 2-benzothiazolylhydrazone in 50 ml of acetic acid, and the solution was allowed to stand at room temperature for 3-4 h. The acetic acid was evaporated *in vacuo*, and the residue was subjected to column chromatography to give a product with R_f 0.62 ($CHCl_3$) and mp 176°C in 35% yield. IR spectrum ($CHCl_3$): 1730, 1710 (C=O); 3388 cm^{-1} (NH). PMR spectrum (d_6-DMSO): 11.18 (1H, s, N–H), 7.2-8.1 (4H, m, aromatic H), 2.72 (1H, septet, C–H), and 1.19 ppm (6H, d, CH_3). Mass spectrum (m/z, relative intensities, %)* (empirical compositions)†: 277 (11), 235 (97) ($C_{11}H_{13}N_3OS$), 206 (12) ($C_9H_8N_3OS$), 192 (13), 165 (100), 151 (43), 149 (32), 123 (28), 105 (39), 85 (34), 71 (72). Found: C 56.0; H 5.4; N 14.8; S 12.0%. $C_{13}H_{15}N_3O_2S$. Calculated: C 56.3; H 5.4; N 15.1; S 11.6%. M 277.0859.

N-Benzoyl-N'-acetyl-N'-(1-benzyl-2-benzimidazolyl)hydrazine (VI). This compound, with R_f 0.9 (ethyl acetate) and mp 214°C, was obtained in 40% yield by a similar method. IR spectrum ($CHCl_3$): 3394 (NH); 1713, 1695 cm^{-1} (C=O). Mass spectrum (m/z, relative intensities, %):* 384 (16), 342 (40), 237 (29), 149 (7), 105 (87), 92 (15), 91 (100), 77 (46). Found: C 71.5; H 5.7; N 14.7%. $C_{23}H_{20}N_4O_2$. Calculated: C 71.9; H 5.2; N 14.6%; M 384.1560.

N-Benzoyl-N'-(2-benzothiazolyl)hydrazine (V). A 2-g (8 mmole) sample of benzaldehyde benzothiazolylhydrazone was dissolved by heating in 50 ml of acetic acid (35-40°C), 2 ml (20 mmole) of n-amyl nitrite was added, and the mixture was refluxed for 3-5 min, after which it was maintained at room tempeature for 2 h. The addition of water as the mixture was stirred vigorously gave a yellow crystalline precipitate. Column chromatography gave a substance with R_f 0.78 ($CHCl_3$) and mp 180°C in 30% yield. IR spectrum ($CHCl_3$): 3390 (NH); 1716, 1678 cm^{-1} (C=O). Mass spectrum (m/z, relative intensities, %)* (empirical compositions):† 269 (23), 164 (10) ($C_7H_6N_3S$), 149 (16), 123 (42), 122 (24), 105 (100) (C_7H_5O), 77 (57). Found: C 62.2; H 3.9; N 15.8; S 11.4%. $C_{14}H_{11}N_3OS$. Calculated: C 62.5; H 4.1; N 15.6; S 11.9%; M 269.0624.

B) A 1-ml (6 mmole) sample of benzoyl chloride was added to a solution of 1 g (6 mmole) of benzothiazolylhydrazine in 170 ml of benzene and 1.5 ml of pyridine, after which the mixture was refluxed for 5 min and maintained at room temperature for 2 h. The benzene was removed by distillation, and the residue was recrystallized from ethanol to give a substance (70%) that was identical to the sample synthesized by method A.

1,4-Dibenzothiazolyl-3,6-diphenyl-1,4-dihydro-1,2,4,5-tetrazine (VII). This compound was isolated along with V by chromatography of the reaction mixture in method A with a column packed with silica gel. Compound VII with R_f 0.48 ($CHCl_3$) and mp 252°C was obtained in 55% yield. UV spectrum (ethanol), λ_{max}: 215 and 335 nm. Mass spectrum (m/z, relative intensities)* (empirical formulas)†: 502 (61), 354 (3) ($C_{21}H_{14}N_4S$), 251 (39) ($C_{14}H_9N_3S$), 250 (11), 237 (44), 148 (100), 134 (49), 122 (6), 103 (19), 90 (26), 77 (33). Found: C 66.8; H 3.8; N 16.6; S 12.8% $C_{28}H_{18}N_6S_2$. Calculated: C 66.9; H 3.8; N 16.7; S 12.8%; M 502.1020.

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*The molecular-ion peaks and 8-10 of the most intense peaks are presented.

†The empirical compositions of the ions were confirmed by the high-resolution mass spectra.