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REACTIONS OF 4-AMINO-1,3,5-DITHIAZINE WITH AMMONIA AND AMINES

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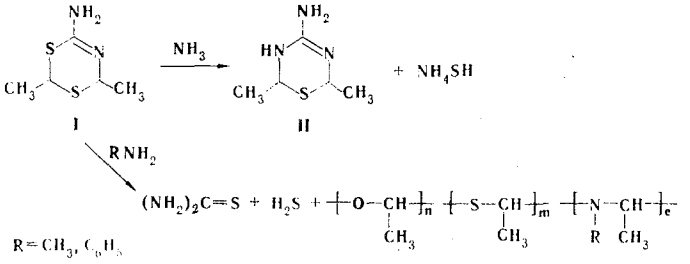
It is shown that selective replacement of the sulfur atom in the 3 position by a nitrogen atom, which leads to 2,6-dimethyl-4-amino-3H-2,6-dihydro-1,3,5-thiadiazine, occurs when 2H,6H-2,6-dimethyl-4-amino-1,3,5-dithiazine is treated with ammonium hydroxide. Under the same conditions, amines cause profound destruction of 2H,6H-2,6-dimethyl-4-amino-1,3,5-dithiazine with the production of thiourea.

Many heterocycles that contain simultaneously nitrogen and sulfur atoms, particularly thiourea derivatives, are unstable with respect to the action of nucleophiles.

According to the data in [1], 2-amino-4-oxo-2-thiazoline undergoes cleavage in aqueous alkaline solutions to give thiourea and 2-hydroxycarboxylic acid. Ring opening, profound decomposition, dimerization, or oxidation may occur when 1,3,4-thiadiazolium salts are treated with bases, depending on the substituents and the conditions [2]. The reaction of 2,4,6-triaryl-4H-1,3,5-thiadiazines with catalytic amounts of aliphatic amines is accompanied by the liberation of elementary sulfur and the formation of 2,4,5-triarylimidazole [3].

The present communication is devoted to a study of the transformations of 2H,6H-2,6-dimethyl-4-amino-1,3,5-dithiazine (I) [4] under the influence of ammonia and amines. As we have already reported [5], in 10-15% aqueous alcohol solutions of ammonia at 20-70°C dithiazine I or its salts (the nitrate and chloride) undergo selective replacement of the sulfur atom in the 3 position by a nitrogen atom to give a new heterocyclic system, viz., 2,6-dimethyl-4-amino-3H-2,6-dihydro-1,3,5-thiadiazine in 62-88% yields.



The PMR spectra of II [6] in various solvents and when the temperature is varied, as well as its IR spectrum [5, 7], provide evidence in favor of the amino form.

In analogy with the reaction presented above, in the reaction of dithiazine I with primary amines (methylamine and aniline) one might have expected the formation of 2,6-dimethyl-3-N-alkyl(aryl)-4-amino-2,6-dihydro-1,3,5-thiadiazine. However, we found that the reaction in this case proceeds with profound decomposition of the starting heteroring to give thiourea, H_2S, and products of condensation of acetaldehyde, thioacetaldehyde, and aldimines, which were not investigated in greater detail. Secondary and tertiary amines in an aqueous alcohol medium give rise to similar decomposition of dithiazine I.

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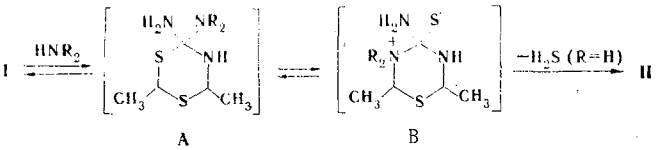
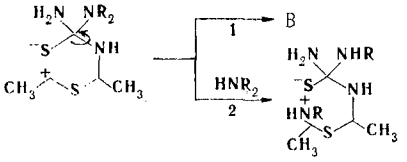
The reactions under consideration evidently commence with addition of ammonia or amines to the C=N bond and the formation of intermediate A, which is capable of undergoing recyclization to intermediate B, which subsequently splits out H_2S to give thiadiazine II.



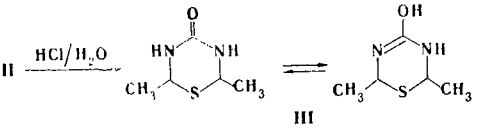
A B

However, competition between the exocyclic NR_2 group (path 1) and the free amine or OH^- ions (path 2) for the resulting carbonium ion should occur in the recyclization step during cleavage of the C_2—S_3 bond.



Path 2 leads to destruction of the ring, which also occurs in the case of amines that are more basic than ammonia ($MeNH_2$, Et_2NH, and Et_3N) [8], the alkyl substituents of which should, moreover, sterically hinder recyclization. The steric reasons evidently become the prevailing factor in the aminolysis of dithiazine I by aniline, which is less basic than ammonia.

In contrast to 2H,6H-2,6-dimethyl-4-amino-1,3,5-dithiazine (I), which is relatively stable in the presence of acids and the salts formed with them [4], 2,6-dimethyl-4-amino-3H-2,6-dihydro-1,3,5-thiadiazine (II) in aqueous acidic media is converted to 2,6-dimethyl-4-oxo-3,5-dihydro-2H,6H,1,3,5-thiadiazine (III). The latter can exist in two tautomeric forms.



III

The IR spectrum of thiadiazine III in the crystalline state contains a set of bands at 3430 and 3230 cm^{-1} (OH, NH) and 2900-2990 cm^{-1} (C—H) and a small peak at 1630 cm^{-1} (C=O). The intense bands at 1520 and 1560 cm^{-1} characterize the C=N group and the N—H deformation vibrations. The band at 1207 cm^{-1} can be assigned to absorption of the C—O bond. The C—S stretching vibrations and the deformation vibrations of the N—H bond lie at 620-650 cm^{-1}. Unfortunately, 1,3,5-thiadiazine III is not soluble in chloroform and CCl_4, and this hinders the study of its tautomerism by means of its IR spectra. A doublet of CH_3 groups at 1.13 ppm and, respectively, a quartet of methylidyne protons of CH—CH_3 fragments and 4.80 ppm with J = 5.5 Hz, as well as a singlet at 8.5 ppm of protons of NH and OH groups, are observed in the PMR spectrum of thiadiazine III in d_6-DMSO. The chemical equivalence of the methylidyne protons indicates an exocyclic orientation of the oxygen atom.

EXPERIMENTAL

The IR spectra of KBr pellets or thin films of the compounds were recorded with a UR-20 spectrometer. The PMR spectra of solutions of the compounds in d_6-DMSO were recorded with a BS 487-C spectrometer (80 MHz) with hexamethyldisiloxane as the internal standard.

2,6-Dimethyl-4-amino-3H-2,6-dihydro-1,3,5-thiadiazine (II). A) A 30-ml sample of 20-25% ammonium hydroxide was added with stirring to a solution of 1.4 g (8.6 mmole) of 2H,6H-2,6-dimethyl-4-amino-1,3,5-dithiazine (I) in 25 ml of ethanol, and the mixture was maintained at 20°C for 2 days. The solvents were removed *in vacuo* to give 1.1 g (85%) of a crystalline compound. Recrystallization from water—ethanol (3:1) gave white shiny needles with mp 188-190°C (dec.). Found: C 41.6; H 7.2; N 28.9; S 22.3%. $C_5H_{11}N_3S$. Calculated: C 41.3; H 7.6; N 28.9; S 22.1%.

B) A 60-ml sample of 20-25% ammonium hydroxide was added to a solution of 1.3 g (8 mmole) of 2H,6H-2,6-dimethyl-4-amino-1,3,5-dithiazine in 10 ml of ethanol, and the mix-

ture was heated at 70-75°C for 3 h and allowed to stand overnight. The precipitated crys. (0.23 g) were removed by filtration, and the mother liquor was worked up to give another 0.8 g of crystalline substance for an overall yield of thiadiazine II of 88%.

C) An 80-ml sample of 20-25% ammonium hydroxide was added with stirring at 40°C to a solution of 2.24 g (10 mmole) of 2H,6H-2,6-dimethyl-4-amino-1,3,5-dithiazinium nitrate in 40 ml of water, and the mixture was maintained at 40°C for 3 h and allowed to stand overnight. It was then evaporated *in vacuo* to 20-30 ml, and the concentrate was cooled. The precipitated crystals were separated, the mother liquor was evaporated, and the residue was washed with cold water and dried to give 0.92 g (62%) of thiadiazine II.

Reaction of Dithiazine I with Methylamine. An 80-ml sample of a 20-25% aqueous solution of methylamine was added to 4.1 g (25 mmole) of dithiazine I in 25 ml of ethanol, and the mixture was maintained at 30-40°C for 10 h and allowed to stand overnight. The solution was evaporated *in vacuo* with collection of the distillate in a cooled trap, and the residue was extracted with CCl_4. Workup of the aqueous layer gave 1.9 g (98%) of thiourea, which was recrystallized twice from ethanol to give a product with mp 179-181°C. The IR spectrum was identical to the spectrum of a genuine sample. Workup of the CCl_4 solution gave a resinous substance that was soluble in water and ethanol. IR spectrum (KBr): 3400 (ν_{NH}), 2800-2960 (ν_{C-H}), 1640 (C=N, δ_{N-H}), and 650 cm^{-1} (C–S). The composition and the spectrum corresponded to the product of condensation of acetaldehyde, thioacetaldehyde, and methylamine in a ratio of ~2:1:1. An aqueous solution of cadmium acetate was added to 70 ml of the aqueous alcohol fraction collected in the trap while cooling with liquid nitrogen, and the resulting orange precipitate was separated and dried to give 1.5 g (41.2%) of CdS.

Reaction of Dithiazine I with Diethylamine. A 6.8-g (90 mmole) sample of diethylamine was added to 2.2 g (13 mmole) of dithiazine I in 25 ml of ethanol, and the mixture was heated at 40-45°C for 8 h and allowed to stand overnight. The solvent and excess amine were removed *in vacuo*, and the residue (3.2 g) was washed with ether (four 30-ml portions) and dissolved in hot dioxane. The dioxane solution was cooled to give 0.75 g (73%) of thiourea with mp 179-181°C. Evaporation of the mother liquor gave 1.4 g of an unidentified powdery compound.

Reaction of Dithiazine I with Triethylamine. A 7.3-g (72 mmole) sample of triethylamine was added to 2.8 g (17 mmole) of dithiazine I in 45 ml of ethanol, and the mixture was heated with stirring at 40-50°C for 10 h and allowed to stand overnight. The ethanol and excess amine were removed *in vacuo*, and the residue (3.3 g) was washed with ether (four 40-ml portions) and dissolved in hot dioxane. The dioxane solution was cooled to give 1.21 g (92%) of thiourea with mp 180-181°C (ethanol). After separation of the thiourea, the dioxane was removed *in vacuo* to give 1.6 g of an unidentified resinous substance.

Reaction of Dithiazine with Aniline. An 8-g (86 mmole) sample of aniline was added to 3.2 g (20 mmole) of dithiazine I, and the mixture was heated with stirring at 40-50°C for 5 h and allowed to stand overnight. The precipitated thiourea (0.2 g) was separated, and the mother liquor was treated with benzene to precipitate another 0.5 g of thiourea for an overall yield of 47% [mp 179-181°C (ethanol)]. An unidentified resinous substance (3.85 g) remained after removal of the benzene and excess aniline *in vacuo*.

2,6-Dimethyl-4-oxo-3,5-dihydro-2H,6H-1,3,5-thiadiazine (III). A mixture of 4 g (27 mmole) of 2,6-dimethyl-4-amino-2,6-dihydro-3H-1,3,5-thiadiazine (II) in 20 ml of water and 40 ml of 5 N HCl was stirred at 40-50°C for 6 h. The resulting precipitate was separated, washed with water, and recrystallized twice from ethanol to give shiny needles with mp 210-211°C (dec.). The yield of thiadiazine III was 2.36 g (59%). Found: C 41.1; H 6.4; N 19.2; S 22.3%. $C_5H_{10}N_2OS$. Calculated: C 41.1; H 6.9; N 19.2; S 21.9%. Workup of the mother liquor gave 1.7 g of NH_4Cl.

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SYNTHESIS OF 2-ETHYNYLAZIRIDINES

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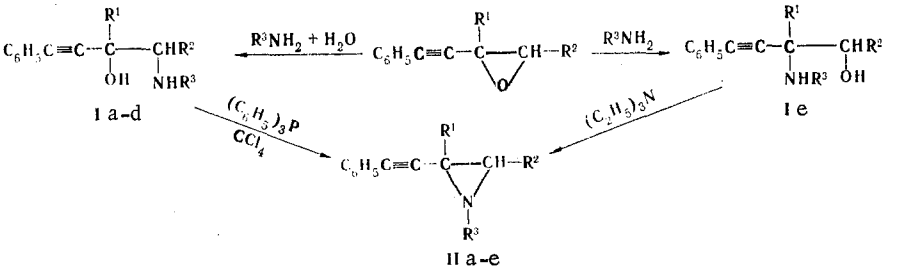
2-Ethynyl-substituted aziridines were obtained by the reaction of acetylenic β-amino and β-azido alcohols with triphenylphosphine and carbon tetrachloride in the presence of triethylamine. The cycloaddition of carbenes and diazomethane to an acetylenic imine was investigated. 2-Ethynylaziridines were obtained in the case of carbonylalkoxycarbenes. The regioselectivity of the cycloaddition of carbenes to an acetylenic imine is demonstrated.

Of the large number of studies dealing with the synthesis and properties of 2-vinylaziridines, thus far only one has been devoted to the synthesis of the corresponding acetylenic aziridine, viz., 2-vinyl-3-ethynylaziridine [1]. At the same time, 2-ethynyl-substituted aziridines are of undoubted interest as valuable intermediates for the preparation of polyfunctional derivatives of aziridine, as well as a number of nitrogen-containing heterocycles.

In the present research we attempted to synthesize compounds of this type on the basis of acetylenic epoxides and acetylenic imines. Methods for the preparation of 2-alkyl- and 2-vinylaziridines by cyclization of the corresponding amino alcohols with triphenylphosphine dibromide or the triphenylphosphine–carbon tetrachloride complex in the presence of triethylamine have been described [1, 2]. We used the latter method for the synthesis of 2-ethynyl-substituted aziridines via the scheme



I, II a $R^1=CH_3$, $R^2=H$, $R^3=C(CH_3)_3$; b $R^1=R^2=CH_3$, $R^3=C(CH_3)_3$; c $R^1=CH_2CH_3$, $R^2=H$, $R^3=CH_2C_6H_5$; d $R^1=H$, $R^2=C\equiv CC_6H_5$, $R^3=C(CH_3)_3$; e $R^1=R^2=CH_3$, $R^3=CH_2C_6H_5$

Starting amino alcohols Ia-e were obtained from acetylenic epoxy compounds and tert-butylamine or benzylamine (Table 1). It should be noted that, depending on the conditions under which the epoxy compounds are opened by amines, two isomers are formed: β-amino alcohols Ia-d are obtained in the presence of small amounts of water, while α-amino alcohol Ie was isolated in the absence of water. The formation of Ie is indicated by resonance ab-

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