# HETEROCYCLIZATION OF COMPOUNDS CONTAINING DIAZO AND CYANO GROUPS.

## 4.* REACTIONS OF 2-DIAZO-2-CYANOACETIC ACID AMIDES WITH $P_4S_{10}$ AND THE LAWESSON REAGENT. SYNTHESIS AND RECYCLIZATION OF 5-AMINO-1,2,3-THIADIAZOLE-4-CARBOTHIOAMIDES

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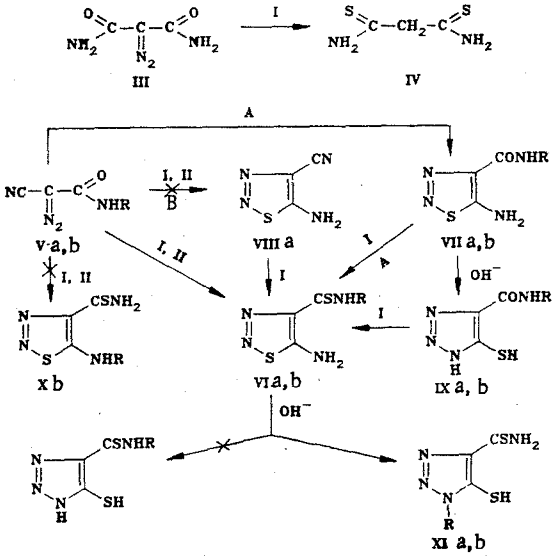
5-Amino-1,2,3-thiadiazole-4-carbothioamides were obtained in the reaction of carbonyl derivatives of diazoacetonitrile with $P_4S_{10}$ and the Lawesson reagent. A novel recyclization of 1,2,3-thiadiazole-4-carbothioamides was observed.

We have previously shown that the reaction of derivatives of 2-diazoacetonitrile with hydrogen sulfide leads to the formation of 2-diazo carbothioamides, which undergo cyclization t 4-substituted 5-amino-1,2,3-thiadiazoles [2], which in basic media undergo recyclization to 5 mercapto-1,2,3-triazoles [2, 3]. It is known [4] that cyclic diazo ketones react with $P_4S_{10}$ (I) and 2,4-bis(4-methoxyphenyl)-1,3,2,4-dithiophosphetane 2,4-disulfide (II, the Lawesson reagent) to give 1,2,3-thiadiazoles [5]. Reactions of aliphatic diazo compounds containing cyano and/or carbamoyl groups with sulfides I and II have not been described. One might have assumed that 2-diazocarbothioamides, which undergo cyclization to either 5-amino-1,2,3-thiadi zoles or 5-mercapto-1,2,3-triazoles, would also be formed in this case.



Va—IXa, XIa R=H; Vb—VIIb, IXb—XIb R=$CH_3$

The subject of the present research was to study the reactions of diazomalondiamide (III) 2-diazoacetonitrile, 2-diazo-2-cyanoacetamide (Va), and -N-methylacetamide (Vb) with sulfides I and II in order to compare the reactivities of diazo, cyano, and carbamoyl groups, to determine the direction of cyclization of the resulting 2-diazo carbothioamides, and to search for new methods for the synthesis of 4-substituted 5-amino-1,2,3-thiadiazoles, which are intermediates in the synthesis of highly active pesticides [6].

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*See [1] for Communication 3.

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Diazomalondiamide (III) and diazoacetonitrile were selected as model compounds that contain two reactive groups. In contrast to cyclic diazo ketones, in the thionation of which condensed 1,2,3-thiadiazoles are formed [5], reductive elimination of the diazo group is observed in the reaction of diazo amide III with sulfide I in dioxane, and malondithioamide (IV) is formed as a result of the subsequent thionation of the two amide groups. According to data from thin-layer chromatography (TLC), a mixture of several compounds, in which 5-amino-1,2,3-thiadiazole is absent, is formed in the thionation of diazoacetonitrile. We were unable to separate this mixture because of the close chromatographic mobilities of the components.

On the basis of these experiments it may be concluded that the diazo group is more active than the carbamoyl and cyano groups in reactions with sulfurating reagents I and II.

The reaction of 2-diazacyanoacetic acid amides Va,b with sulfides I and II proceeds completely differently. It proceeds through thionation of both the carbamoyl and cyano groups and subsequent cyclization of the resulting 2-diazo carbothioamides to 5-amino-1,2,3-thiadiazole-4-carbothioamides VIa,b. Phosphorus-containing organic substances, the IR spectra of which do not contain bands of stretching vibrations of diazo, cyano, and carbamoyl groups, were isolated as intermediates. When they were refluxed in water, they were converted to thioamides VIa,b.

To prove the structure of thiadiazoles VI we carried out the thionation of 5-amino-1,2,3-thiadiazole-4-carboxamides VII, -carbonitrile (VIII), and 5-mercapto-1,2,3-triazoles IX. We observed that under these conditions both amides VII and IX and nitrile VIII undergo smooth conversion to thioamides VI; in the thionation of the thiadiazoles and isomeric triazoles the products are VIa,b, which coincide with one another and with the products of thionation of diazo compounds Va,b with respect to melting points, IR spectra, and TLC data. This can be explained as follows: in addition to thionation, recyclization of the 5-amino-1,2,3-thiadiazoles to 5-mercapto-1,2,3-triazoles or, vice versa, of the triazoles to thiadiazoles occurs. Their 5-amino-1,2,3-thiadiazole structure was established on the basis of mass-spectrometric data. The mass spectra of these substances contain molecular-ion peaks, as well as intense peaks of $[M - N_2]^+$ ions; as we have previously shown [7], this is characteristic for 5-amino-1,2,3-thiadiazoles.

Thus, the reactions of diazo nitriles with sulfides I and II proceed through cyclization of the intermediately formed diazo thioamides to 5-amino-1,2,3-thiadiazoles rather than to 5-mercapto-1,2,3-triazoles; under the same conditions 5-mercapto-1,2,3-triazoles undergo rearrangement to 5-amino-1,2,3-thiadiazoles.

Since 5-amino-1,2,3-thiadiazole-4-carbothioamide (VIa) is formed in the thionation of both thiadiazolecarboxamide VIIa and carbonitrile VIIIa, both pathways (A and B in the scheme) for the conversion of diazo nitrile VA to VIa are equally likely.

In contrast to 2-diazo-2-cyanoacetamide (Va), the formation of both 5-N-methylamino-1,2,3-thiadiazole-4-carbothioamide (Xb) and 5-amino-1,2,3-thiadiazole-4-N-methylcarbothioamide (VIb) or a mixture of them is possible in the thionation of N-methylacetamide VB. However, individual VIb was obtained as a result of this reaction.

Four signals of carbon atoms were recorded in the $^{13}C$ NMR spectrum of thiadiazole VIb (see Fig. 1). On the basis of the data in [8] we assigned the signal at strong field (31.06 ppm) to the carbon atom of a methyl group and the signal resonating at weakest field (184.64 ppm) to the carbon atom of a carbothioamide group. For the assignment of the signals at 167.24 and 136.92 ppm we recorded the spectrum of a genuine sample of 5-amino-1,2,3-thiadiazole obtained by the method in [9]. A doublet of triplets at 130.0420 ppm and a doublet at 165.7864 ppm are observed in its high-resolution spectrum; this makes it possible to assign these signals to the carbon atoms in the 4 and 5 positions, respectively, of the ring. Similarly, the chemical shifts of 136.92 and 167.24 ppm in the spectrum of VIb were assigned to the carbon atoms in the ring 4 and 5 positions. In the high-resolution spectrum of VIb it is apparent that the signal of the carbon atom of the carbothioamide group, in contrast to the carbon atom in the ring 5 position, is split into a quartet with a constant of 4.5 Hz; this constitutes evidence for spin coupling of the carbon atom of the carbothioamide group with the three protons of the methyl group. Thus an analysis of the $^{13}C$ NMR spectra made it possible to unambiguously determine the structure of VIb.

In connection with the fact that the cyclization of diazo thiones proceeds with a low energy barrier, the resulting diazo thione is converted to a 1,2,3-thiadiazole faster than it

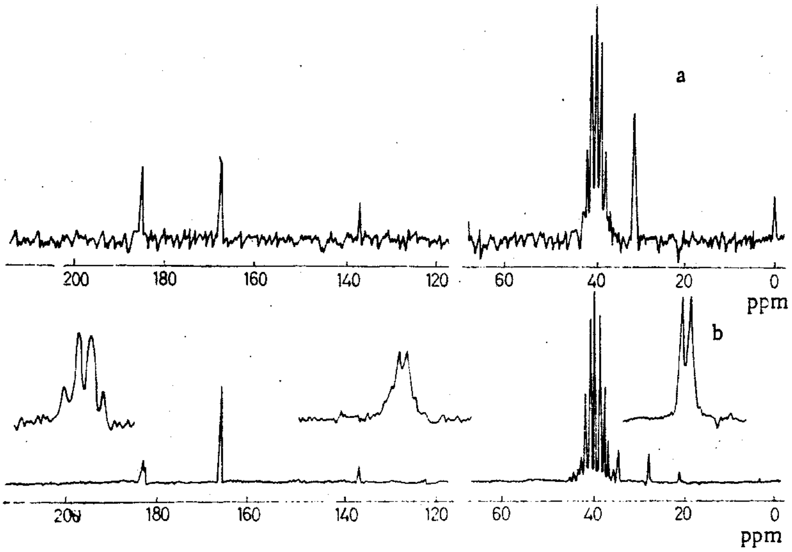

Fig. 1. $^{13}C$ NMR spectrum of 5-amino-1,2,3-thiadiazole-4-N-methylcarbothioamide (VIb): a) with proton decoupling; b) without proton decoupling.

reacts with another molecule of the sulfurating agent. From the structure of the resulting compound one can draw a conclusion regarding the relative reactivities of the cyano and carbamoyl groups in diazo compounds Va,b. Since Vb is converted to thiadiazole VIb, the carbonitrile group has greater reactivity in the reaction, i.e., pathway A is realized (see the scheme). This conclusion is in good agreement with the fact that malondithioamide (IV) is formed in the reaction of diazomalondiamide (III) under similar conditions.

In the reaction of 1,2,3-thiadiazoles VIa,b with aqueous solutions of bases such as alkalis, alkali metal carbonates and bicarbonates, and aliphatic amines one observes their conversion to 5-mercapto-1,2,3-triazoles. However, in contrast to the Dimroth rearrangement described in [10], this process takes place with the participation of the nitrogen atom of the carbothioamide group rather than that of the amino group.

The structure of 5-mercapto-1-N-methyl-1,2,3-triazole-4-carbothioamide (XIb) was confirmed by PMR spectral data. In contrast to N-methylamide IXb, which has a doublet at 3.14 ppm, in the spectrum of XIb the protons of the methyl group appear in the form of a singlet at weaker field (3.9 ppm).

## EXPERIMENTAL

The UV spectra of solutions of the compounds in water at pH 6.5-6.8 were recorded with a Beckmann Model-26 spectrophotometer. The IR spectra of KBr pellets of the compounds were recorded with a UR-20 spectrometer. The PMR spectra of solutions in $d_6$-DMSO were obtained with a Perkin–Elmer R-12B spectrometer (60 MHz) with tetramethylsilane (TMS) as the internal standard. The $^{13}C$ NMR spectra of solutions in $d_6$-DMSO were obtained with a Bruker WP-80 spectrometer (60 MHz) with TMS as the internal standard. The mass spectra were recorded with MAT-311A (ionizing voltage 70 V) and MKh-1303 (50 V) mass spectrometers. The course of the reactions and the purity of the compounds were monitored by TLC on Silufol UV-254 plates in the following solvent systems: chloroform–ethanol (10:1) ($Rf_1$), chloroform–methanol–acetic acid (30:1:1) ($Rf_2$), propanol–3 N ammonium hydroxide (3:1) ($Rf_3$), and chloroform–ethanol (3:1) ($Rf_4$).

5-Amino-1,2,3-thiadiazole-4-carbothioamide (VIa). A) A 2-g (4.5 mmole) sample of $P_4S_{10}$ was added with vigorous stirring at 50°C to a suspension of 1 g (9 mmole) of diazo compound Va in 10 ml of absolute dioxane, after which the temperature was raised to 100°C, and the reaction mixture was maintained at this temperature for 1 h. The precipitate was removed by filtration, and the filtrate was evaporated to dryness. The residue was extracted with boiling water, the aqueous extract was cooled, and the resulting precipitate was removed by filtration and crystallized from water with charcoal to give 0.5 g (34%) of light-yellow crystals with mp 171-172°C, $Rf_1$ 0.25, $Rf_2$ 0.31 and $Rf_4$ 0.91. IR spectrum: 3400, 3300, and 3190 $cm^{-1}$ ($NH_2$). Mass spectrum, m/z (%): $M^+$ 160 (100), 132 (33), 105 (33), and 67 (26). UV spectrum,

$\lambda_{max}$ (log ε): 2.5 (4.15), 275 (4.21), and 315 nm (414). Found, %: C 22.75, H 2.56, N 34.87, S 39.84. $C_3H_4N_4S_2$. Calculated, %: C 22.5, H 2.5, N 35.0, S 40.0.

B) A 3.7-g (9 mmole) sample of the Lawesson reagent was added to a solution of 1 g (9 mmole) of diazo compound Va in 10 ml of absolute dioxane, and the mixture was refluxed for 2 h. The solution was evaporated, and the oily residue was extracted with hot water and the addition of charcoal. The extract was cooled, and the resulting resin was crystallized twice from water. The yield was 0.6 g (42%). With respect to its melting point, TLC data, and UV, IR, and PMR spectrometric data, the reaction product was identical to thiadiazole VIa obtained by method A.

5-Amino-1,2,3-thiadiazole-4-N-methylcarbothioamide (VIb). A) This compound was obtained by method A for VIa. The yield was 25%. The product had mp 185°C, $Rf_1$ 0.58, $Rf_2$ 0.49 and $Rf_4$ 0.55. IR spectrum: 3300, 3200 $cm^{-1}$ ($NH_2$). PMR spectrum: 3.14 (3H, d, J = 5.5 Hz, $CH_3$) and 8.92 ppm (2H, s, $NH_2$). $^{13}C$ NMR spectrum: 31.06 [1H, 3H, q, d, $^1J(CH_3)$ = 11.23, $^3J(NH,C)$ 3.05 Hz, $NHCH_3$], 136.92 [3H, q, $^4J(CH_3)$ = 3.37 Hz, $C_{(4)}$], 167.24 [s, $C_{(5)}$]. and 184.66 ppm [3H, q, $^2J(CH_3)$ = 4.98 Hz, C=S]. Mass spectrum, m/z (%): $M^+$ 174 (100), 117 (20), 105 (24), and 74 (17). UV spectrum, $\lambda_{max}$ (log ε): 213 (4.16), 275 (4.23), and 305 nm (4.06). Found, %: C 27.9, H 3.29, N 31.97, S 36.33. $C_4H_6N_4S_2$. Calculated, %: C 27.59, H 3.45, N 32.18, S 36.78.

B) This compound was obtained by method B for VIa. The yield was 18%. With respect to its melting point, TLC data, and UV, IR, and PMR spectrometric data, the product was identical to the thiadiazole obtained by method A.

5-Mercapto-1,2,3-triazole-4-carbothioamide (XIa). A 0.15-g (0.9 mmole) sample of thiadiazole VIa was dissolved in 5 ml of 25% ammonium hydroxide, and the solution was refluxed for 30 min. It was then cooled and acidified to pH 2, and the precipitate was removed by filtration and crystallized from water. The yield was 0.13 g (86.7%). The product had mp 208°C, $Rf_3$ 0.59, and $Rf_4$ 0.83. IR spectrum: 3390, 3200 $cm^{-1}$ ($NH_2$). Mass spectrum, m/z (%): $M^+$ 160 (100), 143 (16), 127 (20), and 60 (24). UV spectrum, $\lambda_{max}$ (log ε): 213 (4.21), 265 (3.96), and 336 nm (4.20). Found, %: C 22.76, H 2.35, N 34.95, S 40.52. $C_3H_4N_4S_2$. Calculated, %: C 22.5, H 2.5, N 35.0, S 40.0.

1-N-Methyl-5-mercapto-1,2,3-triazole-4-carbothioamide (XIb). This compound was obtained by a procedure similar to that used to prepare XIa. The yield was 98%. The product had mp 147°C, $Rf_2$ 0.15, $Rf_3$ 0.75, and $Rf_4$ 0.59. IR spectrum: 3265, 3210 $cm^{-1}$ ($NH_2$). PMR spectrum: 3.90 ppm (3H, s, $CH_3$). Mass spectrum, m/z (%): $M^+$ 174 (100), 105 (9), 81 (13), and 60 (14). UV spectrum, $\lambda_{max}$ (log ε): 215 (4.18), 267 (3.92), and 335 nm (4.16). Found, %: C 28.2, H 3.6, N 32.4, S 36.5. $C_4H_6N_4S_2$. Calculated, %: C 27.6, H 3.45, N 32.2, S 36.8.

Malondithioamide (IV). This compound was obtained by method A for VIa. The yield was 33%. The product had mp 209°C (mp 211-212° [11]). Mass spectrum, m/z (%): $M^+$ 134 (100), 101 (20), 100 (40), 60 (68), and 66 (10).

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