7. C. D. Hurd and L. J. Gershbein, J. Amer. Chem. Soc., 69, 28 (1947).
8. G. Miyajima, K. Takahashi, and K. Nishimoto, Org. Magn. Reson., 6, 413 (1974).
9. J. J. Amico, J. Amer. Chem. Soc., 79, 5270 (1957).
10. N. A. Aliev, R. Aflyatunova, and K. Giyasov, in: Fungicides [in Russian], Fan, Tashkent (1980), p. 53.
11. K. V. Anan'eva and N. K. Rozhkova, All-Union Institute of Scientific and Technical Information, Academy of Sciences of the USSR, deposited paper No. 239-71; Ref. Zh. Khim., 9Zh99 (1972).

HETEROCYCLIZATION OF COMPOUNDS CONTAINING DIAZO AND CYANO GROUPS.

2.* SYNTHESIS AND RECYCLIZATION OF 4-SUBSTITUTED 5-AMINO-1,2,3-THIADIAZOLES

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The reaction of carbonyl derivatives of diazoacetonitrile with hydrogen sulfide in the presence of triethylamine yields 4-substituted 5-amino-1,2,3-triadiazoles. Under analogous conditions, hydrogen selenide and ethyl mercaptan reduce the starting diazo compounds to hydrazones. Thiadiazoles are recyclized to 4-substituted 5-mercapto-1,2,3-triazoles by the action of bases.

In our previous work [1], we showed that the reaction of carbonyl derivatives of diazoacetonitrile with hydrogen halides leads to the formation of 4-substituted 5-halo-1H-1,2,3-triazoles. In the present communication, we studied the reactions of diazoacetonitriles with hydrogen sulfide and hydrogen selenide in order to obtain 4-substituted 5-amino-1,2,3-thiadiazoles, which are starting reagents for the preparation of various pesticides [2, 3] and their selenium analogs.

Diazoacetonitrile and its alkyl and aryl derivatives react with hydrogen sulfide in the presence of bases to form 5-amino-1,2,3-triadiazoles [4, 5]. In addition, the reaction of carbonyl derivatives of diazomethane with hydrogen sulfide, depending on the substituents, gives either thionylation of the carbonyl group with subsequent cyclization to 1,2,3-thiadiazole or reduction of the diazo compounds to hydrazones [6]. Thus, the formation of three different products may be expected in the reaction of carbonyl derivatives of diazoacetonitrile with hydrogen sulfide.

However, the only products of the reaction of 2-diazo-2-cyanoethyl acetate (Ia), 2-diazo-2-cyanoethylacetamide (Ib), 2-diazo-2-cyanoethyl-N-methylacetamide (Ic) and 2-diazo-2-cyanoethylacetophenone (Id) with hydrogen sulfide in the presence of triethylamine were 4-substituted 5-amino-1,2,3-thiadiazoles (IIa-d). The sturcture of thiadiazoles IIa-d was confirmed by IR, UV, and PMR spectroscopy and by the convergent synthesis of IIa and IId according to Goerdeler [7]. Thus, only the first of the three possible reaction pathways obtains.

We should note that formation of 5-amino-1,2,3-thidiazoles in this reaction may proceed by two different mechanisms, either through the α-diazothioamide or through the α-cyanothiadiazene with subsequent cyclization of these kinetically unstable intermediates. In order to distinguish between these two mechanisms, we carried out a comparative kinetic study of the reactions of 2-diazo-2-cyanoacetamide Ib and a compound with similar electronic structure but incapable of reacting through the first mechanism with hydrogen sulfide. 2-Diazomalondiamide III was taken as this model.

*For 1, see [1].

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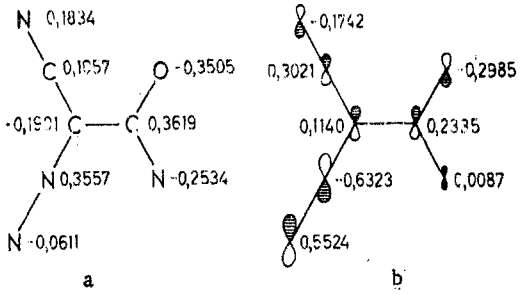


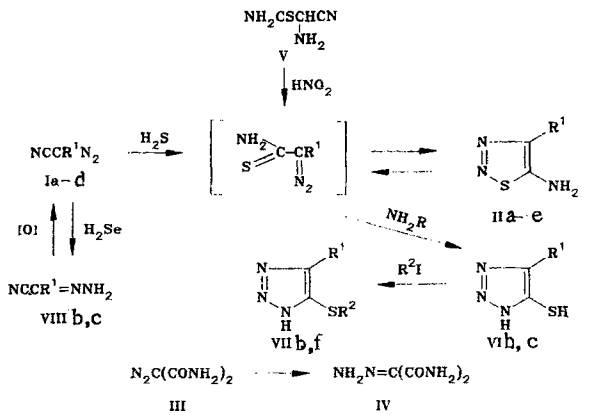
Fig. 1. Calculation of the charge distribution (a) and LUMO coefficients (b) of 2-diazo-2-cyanoacetamide.

TABLE 1. Properties of the Compounds Synthesized

Compound	mp.[a] °C	R_f 10² A	R_f 10² B	R_f 10² B	Found, % C	Found, % H	Found, % N	Found, % S	Chemical formula	Calculated, % C	Calculated, % H	Calculated, % N	Calculated, % S	Yield, %
IIa	125—126[b]	88	84	85	34,9	4,3	24,5	18,6	$C_5H_7N_3O_2S$	34,7	4,1	24,3	18,5	34
IIb	178—179[c]	68	63	73	25,1	2,9	38,9	22,5	$C_3H_4N_4OS$	25,0	2,8	38,9	22,2	81
IIc	210—211	52	79	78	30,4	3,9	35,3	20,3	$C_4H_6N_4OS$	30,4	3,8	35,4	20,3	30
IId	160[d]	—	77	—	—	—	20,6	15,6	$C_9H_7N_3OS$	52,7	3,4	20,5	15,6	51
IIe	165—166[e]	41	81	86	28,4	1,7	44,6	25,6	$C_3H_2N_4S$	28,6	1,6	44,4	25,4	51
IV	178	20	58	57	28,1	4,7	42,9	—	$C_3H_6N_4O_2$	27,7	4,6	43,1	—	89
VIb	207—208	55	71	87	25,1	2,8	39,0	22,5	$C_3H_4N_4OS$	25,0	2,8	38,9	22,2	97
VIc	202—204	77	90	90	28,9	4,5	33,9	19,1	$C_4H_6N_4OS \times 0{,}5H_2O$	28,7	4,2	33,5	19,2	95 (A) 75 (B)
VIIb	257—259	33	64	71	30,1	3,9	35,5	20.3	$C_4H_6N_4OS$	30,4	3,8	35,4	20,3	82
VIIf	172—175	31	71	60	32,0	4,3	34,5	18,7	$C_5H_8N_4OS$	34,9	4,7	32,5	18,6	64
VIIIb	170—171	—	41	86	32,4	3,8	49,7	—	$C_3H_4N_4O$	32,1	3,6	50,0	—	27

[a] mp not corrected; IIa-c, e, VIIb, f, and VIIIb were recrystallized from water, IId from $CHCl_3$—hexane, IVb, c from ethanol, and IV was precipitated from 10 N citric acid by the addition of sodium carbonate. [b] mp 126°C (subl.) [7]. [c] Without decomposition. [d] mp 160°C [7]. [e] mp 168-171°C (from CH_3CN).

UV spectroscopy indicated that the time for 50% conversion of diazoamide Ib in the case of $2.2 \cdot 10^{-4}$ mole/liter initial concentration in the presence of an equimolar amount of triethylamine and $4 \cdot 10^{-3}$ mole/liter hydrogen sulfide in absolute ethanol is 9 min. The family of kinetic curves transverses an isosbestic point, indicating that neither side-products nor intermediates for formed during the reaction in any significant concentration. Under analogous conditions, diazodiamide III remains unchanged over two months.



I, II a R^1=COOEt, d R^1=COPh; II e R^1=CN; I, II, VI—VIII b R^1=$CONH_2$, R^2=—Me, f R^2=Et; I, II, VI, VIII c R^1=CONHMe

When the concentrations of the diazo compound and triethylamine are increased to 0.01 mole/liter, diazonitrile Ib reacts with hydrogen sulfide virtually instantaneously. On the other hand, the reaction of diazodiamide III with excess hydrogen sulfide is complete only after 22 h with the formation of only 2-hydrazonomalonodiamide (IV).

Such a sharp difference in the rates of the reactions of diazonitrile Ib and diazodiamide III with hydrogen sulfide may be attributed only to the formation of different inter-

TABLE 2. Spectral Indices of Compounds Synthesized

Compound	IR spectrum (KBr), cm^{-1}		UV spectrum (in water), λ_{max}, nm (log ε)	PMR spectrum (in DMSO-d_6), δ, ppm
	stretching	deform.		
IIa	3275, 3220, 3150 (NH), 1690 (CO)	1530 (NH)	262 (3,90), 284 (sh., 3,78)	8,4 (2H, s, NH_2), 4,45 (2H, q, J=7,8 Hz, CH_2), 1,36 (3H, t, J=7,8 Hz, CH_3)
IIb	3380, 3305, 3270, 3200 (NH), 1675 (CO)	1520 (NH)	260 (3,99), 291 (3,89)	
IIc	3400, 3250 (NH), 1645 (CO)	1515 (NH)	258 (3,35), 283 (3,78)	9,0 (1H, s, NH), 8,52 (2H, s, NH_2), 2,96 (3H, d, J=6,0 Hz, $NHCH_3$)
IIe	3420, 3320, 3220 (NH), 2250 (CN)	1525 (NH)	247 (3,66), 292 (3,63)[a]	
IV	3475, 3390 (NH), 1705 (CO)		275 (3,97)[a]	
VIb	3420, 3340 (NH), 1670 (CO)	1565, 1530 (NH)	256 (4,03)	
VIc	3240, 3155 (NH), 1650 (CO)	1550 (NH) 775 (SH)	258 (4,00)	8,95 (s, NH), 2.84 (s, NCH_3), 2,84 (d, J=7,3 Hz, $NHCH_3$)
VIIb	3385, 3285, 3235 (NH), 1675 (CO)	1555 (NH)	233 (sh., 3,69), 263 (3,53)[a]	7,63 (1H, s, NH), 7,40 (1H, s, NH), 2,49 (3H, s, SCH_3)
VIIf	3390, 3290, 3235 (NH), 1680 (CO)	1570 (NH)	233 (sh., 3,71), 262 (3,69)	8,3—7,1 (3H, NH), 3,04 (2H, q, J=7,2 Hz, SCH_2), 1,25 (3H, t, J=7,2 Hz, CH_3)
VIIIb	3400, 3345, 3240, 3160 (NH), 2235 (CN), 1710 (CO)	1520 (NH)	230 (3,64), 286 (4,09)[a]	
VIIIc	3390, 3320, 3220 (NH), 2220 (CN)		245 (sh, 3,69), 286 (4,02)	8,1 (1H, s, NH), 2,72 (3H, d, J=4,8 Hz, $NHCH_3$)

[a]In ethanol.

mediates (an α-diazothioamide, which rapidly cyclizes to thiadiazole IIb [8], and a thiadiazene, respectively) or a much greater rate for the cyclization of the thiadiazene than for its decomposition to the hydrazone and sulfur. However, in this latter case, the thiadiazene should accumulate in the solution. Thus, the reaction of diazonitriles I with hydrogen sulfide apparently proceed through the formation of α-diazothioamides.

The conclusion of the reaction of hydrogen sulfide with diazonitrile I at the cyano group requires further evidence, since there is not information in the literature on the direction of the cyclization of the diazothioamides formed in this case which contain electron-withdrawing substituents in the α-position (either at the sulfur atom or at the nitrogen atom of the thioamide group). Experimental evidence was found in the reported generation of this system upon the diazotrization of 2-amino-2-cyanothioacetamide (V). In our previous work [9], we found that the only product of this reaction is 5-amino-1,2,3-thiadiazole-4-carbonitrile (IIe) which was identical to this compound synthesized previously by Volpp [2] by an independent method. Thus, α-diazothioamides may be found on the coordinate of the reaction of diazonitriles I with hydrogen sulfide.

However, under more vigorous conditions, the α-diazothioamides formed upon heating thiadiazoles IIa-c at reflux in excess aqueous ammonia or methylamine cyclize to give isomeric 5-mercapto-1H-1,2,3-triazole-4-carboxamide (VIb) and the corresponding N-methylcarboxamide (VIc), respectively. The recyclization of ester IIa is accompanied by the amidation of the ester group. In contrast to the starting thiadiazoles II, mercaptotriazoles VIb and VIc give a rapidly disappearing green-blue color with aqueous ferric chloride, indicating the presence of a free mercapto group [10]. In order to confirm the structure of mercaptotria-

zoles VIb and VIc, we carried out the alkylation of mercaptotriazole VIb with methyl iodide and ethyl iodide. The PMR signals for the methyl and methylene group protons in the products 5-methyl- (VIIb) and 5-ethylthio-1H-1,2,3-triazole-4-carboxamide (VIIf) are at 2.49 and 3.04 ppm, which is characteristic for alkylthio groups.

In order to address the second aspect of this work, we studied the reaction of diazonitriles I with hydrogen selenide. However, in this case, we isolated pure compounds which, on the basis of their IR spectra and elemental analysis, were identified as 2-hydrazono-2-cyanoacetamide (VIIb) and the corresponding N-methylacetamide (VIIIc) instead of selenadiazoles. Under analogous conditions, diazonitrile Ia forms a mixture of strongly colored products which could not be separated due to their similar chromatographic mobilities. The structures of hydrazones VIIIb and VIIIc were indicated by their oxidation using lead tetraacetate to the starting diazo compounds Ib and Ic.

In an attempt to obtain 5-ethylthio-1H-1,2,3-triazole-4-carboxamide (VIIf) from diazoamide Ib, we found that this compound does not react with ethyl mercaptan upon heating at reflux in chloroform. Heating of the reaction mixture at 100°C for 12 h in an autoclave leads to a mixture of seven products as indicated by thin-layer chromatography. None of these compounds corresponds in its chromatographic mobility with ethylmercaptotriazole VIIf or hydrazone VIIIb. On the other hand, diazoamide Ib reacts rapidly in ethanol with ethyl mercaptan in the presence of triethylamine at room temperature but hydrazone VIIIb rather than triazole VIIc is formed in this case.

We carried out quantum chemical calculations for the reactivity indices of 2-diazo-2-cyanoacetamide (Ib) using the CNDO/2 approximation and the VIKING program set. The neutral diazoamide molecule Ib was selected as the model since the UV and IR spectra of diazonitriles Ib and Id remain unaltered upon the addition of triethylamine, whose role thus reduces to anionic activation of the nucleophilic reagents.

These calculations account for the preference of the attack of hydrogen sulfide at the nitrile carbon atom. In other cases, electrophilic attack at the diazo group is preferred, leading to reduction to a hydrazone.

Thus, these experiments and quantum chemical calculations indicate the double reactivity of carbonyl derivatives of diazoacetonitrile.

EXPERIMENTAL

The UV spectra were taken on a Beckman Model 26 spectrometer in water at pH 6.5-6.8 and ethanol. The IR spectra were taken on UR-20, Specord IR-75, and Beckman IR-4260 spectrometers in KBr pellets. The PMR spectra were taken on a Perkin-Elmer R-12B spectrometer at 60 MHz in DMSO-d_6 with HMDS as the internal standard. The reactions were monitored and purity of the compounds separated was checked by thin-layer chromatography on Silufol UV-254 plates using 9:1 chloroform—ethanol (A), 3:1 propanol—3 N ammonia (B) and 4:1:1:1 butanol—acetic acid—water—ethyl acetate (C) as eluents. The diazo compounds were determined by the color reaction of their chromatographic spots upon spraying the chromatograms with ethanolic m-phenylenediamine.

The characteristics of the compounds synthesized are given in Tables 1 and 2.

5-Amino-1,2,3-thiadizaoles IIa-d. Hydrogen sulfide was introduced into a solution of 5.56 g (40 mmoles) diazoester Ia or 4 mmoles diazo compounds Ib-d and an equimolar amount of triethylamine in 500 ml chloroform at 20-25°C until diazo compounds Ia-d disappeared. The reaction mixture was evaporated in vacuum to dryness, and the residue was crystallized to give light yellow crystals.

2-Hydrazonomalonodiazmide (IV). Hydrogen sulfide was introduced into a solution of 0.3 g (2.34 mmoles) 2-diazomalondiamide (III) and 0.33 ml (2.34 mmoles) triethylamine in a mixture of 180 ml chloroform and 40 ml ethanol at room temperature for 75 min. After 22 h, the solvent was evaporated and the dry residue was treated with two 20-ml portions of ethanol. Sulfur was filtered off and the filtrate was evaporated in vacuum to dryness. The residue was reprecipitated from ethanol to give colorless needles.

5-Amino-1,2,3-thiadiazole-4-carbonitrile (IIe). A sample of 20 ml ether was added to a solution of 0.4 g (3.48 mmoles) amine V and 36 ml 2 N hydrochloric acid and then a solution of 0.5 mg (5.79 mmoles) KNO_2 in 2 ml water was added with stirring at 0-2°C. The layers were separated and the aqueous layer was extracted with five 20-ml portions of ether. The ethereal

extracts were combined and evaporated to dryness. The residue was crystallized to give light yellow crystals.

5-Mercapto-1H-1,2,3-triazole-4-carboxamide (VIb). A solution of 0.5 g (3.47 mmoles) thiadiazole IIb in 20 ml 25% aqueous ammonia was heated at reflux for 15 min. The solvent was evaporated in vacuum to 50% volume and the pH was brought to 6 by the addition of sulfuric acid. The solution was evaporated to dryness and the residue was crystallized to give light yellow crystals.

5-Mercapto-1H-1,2,3-traizole-4-N-methylcarboxamide (VIc). A. A solution of 0.1 g (0.63 mmole) thiadiazole IIc in 5 ml 25% aqueous ammonia was heated at reflux for 15 min and treated analogously to the procedure for VIb to give colorless needles.

B. This product was obtained by analogy to method A from 0.6 g (3.46 mmoles) ester IIa and 15 ml 22% aqueous methylamine. The product was identical to that obtained by method A in its IR spectrum and melting point.

5-Alkylthio-1H-1,2,3-triazole-4-carboxamides (VIIb). A sample of 6.6 mmoles methyl iodide or ethyl iodide was added to a solution of 0.476 g (2.3 mmoles) diazoamide Ib and 0.124 g (2.3 mmoles) sodium methylate in 8 ml methanol. After 15 min, the solvent was evaporated in vacuum to dryness and the residue was crystallized to give light yellow crystals.

2-Hydrazono-2-cyanoacetamide (VIIIb). A Hydrogen selenide was introduced into a solution of 4 mmoles diaozamide Ib or Ic and an equimolar amount of triethylamine in 200 ml chloroform at 20-25°C until the complete disappearance of the diazo compound. The reaction mixture was maintained for 2 h and amorphous selenium was filtered off. The filtrate was evaporated in vacuum to dryness and the residue was crystallized to give light yellow or light brown crystals which darken over time in the air.

B. A sample of 0.60 ml (8 mmoles) ethyl mercaptan was added with stirring to a solution of 4 mmoles diazoamide Ib or Ic and 0.14 ml (4 mmoles) triethylamine in 10 ml ethanol. The solvent was evaporated in vacuum to dryness and the residue was crystallized. The products obtained were identical in their IR spectra and melting points to the products obtained by method A.

Oxidation of 2-Hydrazono-2-cyanoacetamides. Lead tetraacetate was added in small portions to an aqueous solution of hydrazone VIIb or VIIc until a black precipitate began to form. The reaction mixture was cooled and diazoamide Ib or Ic was extracted with ether and evaporated. The oxidation products were identical in their IR spectra and thin-layer chromatographic behavior with diazo compounds Ib and Ic, respectively.

LITERATURE CITED

1. Yu. M. Shafran, V. A. Bakulyaev, V. S. Mokrushin, and S. G. Alekseev, Khim. Geterotsikl. Soedin., No. 9, 1266 (1984).
2. G. P. Volpp and H. Dounchis, US Patent No. 3,723,448; Chem. Abstr., 79, 5345 (1973).
3. H. Schultz and F. Arndt, West German Patent No. 2,214,632; Chem. Abstr., 80, 14931 (1974).
4. N. V. Konstantinova, USSR Inventor's Certificate No. 956,476; Byul. Izobr., No. 33 (1982).
5. M. Nakai, K. Harada, and Y. Mori, US Patent No. 4,269,982; Chem. Abstr., 95, 62231 (1981).
6. P. P. Norton and S. Shyam, J. Heterocycl. Chem., 12, 1191 (1975).
7. J. Goerdeler and G. Gnad, Chem. Ber., 99, 1618 (1966).
8. R. Huisgen, Khim. Geterotsikl. Soedin., No. 5, 579 (1981).
9. Yu. M. Shafran, V. A. Bakulev, V. S. Mokrushin, and P. N. Kondrat'ev, USSR Inventor's Certificate No. 1,055,741; Byul. Izobr., No. 43 (1983).
10. M. Regitz and A. Liedhegener, Ann., 710, 118 (1967).