3. O. Aki and V. Nakagawa, Chem. Pharm. Bull., 20, 1325 (1972).
4. M. Mazharuddin and G. Thyagarajan, Tetrahedron Lett., No. 4, 307 (1971).
5. M. R. Chandramohan and S. Seshadri, Indian J. Chem., 12, 240 (1974).
6. A. R. Katritzky, Physical Methods in the Chemistry of Heterocyclic Compounds, Academic Press, London (1963).
7. B. Hansen and H. Dobeneck, Chem. Ber., 105, 3630 (1972).
8. A. Mannschreck and U. Koelle, Tetrahedron Lett., No. 10, 863 (1967).
9. A. N. Kost, P. A. Sharbatyan, P. B. Terent'ev, Z. F. Solomko, V. S. Tkachenko, and L. G. Gergel', Zh. Org. Khim., 8, 2113 (1972).
10. A. Mannschreck, G. Rissmann, F. Vögtle, and D. Wild, Chem. Ber., 100, 335 (1967).
11. N. S. Prostakov, A. T. Soldatenkov, M. V. Bagdadi, A. A. Fomichev, and N. I. Golovtsov, Khim. Geterotsikl. Soedin., No. 9, 1238 (1982).
12. N. N. Bychikhina, V. A. Azimov, and L. N. Yakhontov, Khim. Geterotsikl. Soedin., No. 3, 356 (1982).
13. T. S. Chmilenko, Z. F. Solomko, and A. N. Kost, Khim. Geterotsikl. Soedin., No. 4, 525 (1977).

HETEROCYCLIC COMPOUNDS CONTAINING DIAZO AND CYANO GROUPS.

1. DIAZOACETONITRILE DERIVATIVES IN THE SYNTHESIS OF 5-HALO-1H-1,2,3-TRIAZOLES

Yu. M. Shafran, V. A. Bakulev, V. S. Mokrushin,
and S. G. Alekseev

UDC 547.467.2'791

Carbonyl-substituted derivatives of diazoacetonitrile have been obtained by the diazotization of amines and by diazo-group transfer which, under the action of hydrogen halide, have been converted into 4-carbonyl-substituted 5-halo-1H-1,2,3-triazoles. The structures of these compounds have been confirmed by mass spectrometry and independent synthesis.

The cyclization of diazo compounds having a cyano group in the α position under the action of nucleophilic reagents is represented only by the reaction of alkyl and phenyl derivatives of diazoacetonitrile with hydrogen sulfide [1]. At the same time, it may be expected that other diazoacetonitrile derivatives would also take part in various addition reactions at the nitrile group with the formation of heteroanalogs of the pentadientyl anion cyclizing to five-membered heterocycles.

The present communication is devoted to an investigation of the reactions of derivatives of 2-carbonyl-2-diazoacetonitrile (I) with hydrogen halides.

The initial ethyl 2-cyano-2-diazoacetate (Ia) and the corresponding acetamide (Ib) and N-methylacetamide (Ic) were obtained by the diazotization of the corresponding amines (IIa-c), and the acetophenone (Id) by a diazo-group transfer reaction to benzoylacetonitrile (IId) [2].

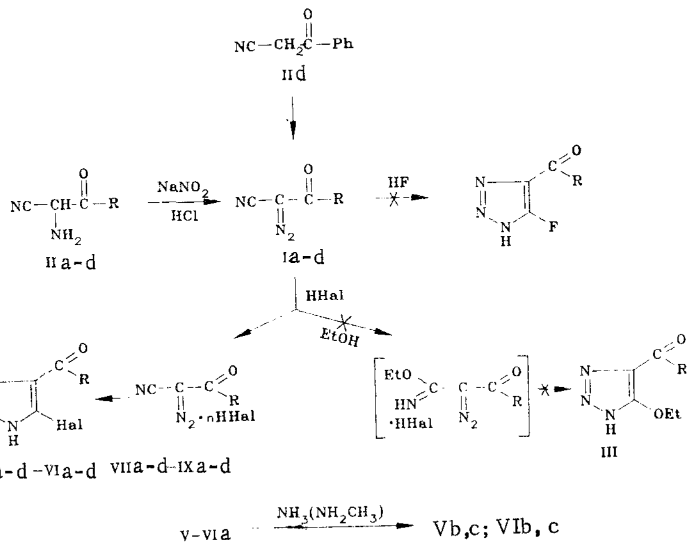
It has been shown previously [3] that diazomalononitrile does not react with hydrogen chloride. We have found that, in contrast to diazomalononitrile, the diazonitriles (Ia-d) react with hydrogen chloride, bromide, and iodide but, instead of the ethoxytriazoles (III), this process forms the 5-halo-1H-1,2,3-triazoles (IV-VI). The replacement of the solvent by chloroform or hexane did not change the nature of the products of this reaction.

The IR spectra of each of the triazoles (IV-VI) contained absorption bands at 3540-3350 cm^{-1} (NH) and 1730-1640 cm^{-1} (CO), and lacked absorption bands characteristic for C≡N and N≡N bonds (Table 1). In the mass spectra of the ester (IVa) and of the amide (IVb) the peaks

---

S. M. Kirov Ural Polytechnic Institute, Sverdlovsk. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 9, pp. 1266-1270, September, 1984. Original article submitted November 6, 1983; revision submitted April 20, 1984.

0009-3122/84/2009-1038$08.50



I—IX, a R=OEt; b R=NH$_2$; c R=NHCH$_3$; d R=Ph; IV, VIIa—d Hal=Cl; V, VIIIa—d Hal=Br; VI, IXa—d Hal=I, n=1, 2

of the molecular ions (M^+) with m/z 175, 177 and 146, 148, respectively, were recorded. The isotopic distribution of M^+ showed the presence of one chlorine atom in it, and the fragmentation of M^+ the presence in it of a fragment containing an N—N bond, which confirmed the structure of the chlorotriazoles (IV). The synthesis of ethyl 5-chloro-12,3-triazole-4-carboxylate (IVa) has been described in [5, 6], somewhat later than our report [4]. The IR spectra and melting points given in [5, 6] and those which we determined for the ester (IVa) coincide.

When hydrogen halides were passed into chloroform solutions of the diazoacetonitriles (Ia-d), first a precipitate of the adducts (VIIa-d)-(IXa-d) deposited very rapidly. The IR spectra of these compounds showed absorption bands at 2235-2225 cm^{-1} (C≡N), 2145-2135 cm^{-1} (N≡N), and 1710-1650 cm^{-1} (C=O). On the basis of the IR spectra and the results of TLC [identical Rf values of the adducts (VIIa-d)-(IXa-d) and of the initial diazo nitriles (Ia-d)] and elementary analysis, the compounds (VIIa-d)-(IXa-d) were assigned the structure of the hydrohalides of the diazo nitriles (Ia-d). The hydrogen halides (VIIa-d)-(IXa-d) had variable compositions, while the hydrobromides (VIIIa-d) and the hydriodides (IXa-d) were rapidly oxidized by atmospheric oxygen. On storage in the solid state at room temperature, the hydrochloride (VIIb) and the dihydrobromide (VIIIb) changed spontaneously into the triazoles (IVb) and (Vb). The isolation of the dihydriodide (IXb) and its subsequent heating in the absence of oxygen was the only method for obtaining the iodotriazole (VId) from the diazo amide (Ib), since in suspension the dihydriodide (VIc) rapidly suffered the elimination of nitrogen and the saponification of the cyano group, which led to its conversion into malondiamide.

In the PMR spectra of the methylamides (Ic) and (IVc-VIc) in DMSO-D$_6$, the signal of the protons of the methyl group appeared in the form of a doublet with a SSCC of 4.8 Hz because of splitting on the proton of the amide nitrogen. When CD$_3$OD was added to the cell of the spectrometer, the SSCC fell sharply because of the replacement amide hydrogen atom by deuterium, as a result of which the signal of the methyl group was converted into a broadened singlet.

When the ethyl esters (Va) and (VIa) were treated with aqueous solutions of ammonia and methylamine, amidation of the ester group took place with the formation of the halotriazolecarbonamides (Vb, c) and (VIc), respectively. No nucleophilic exchange of the halogen atom took place even when the halotriazoles (IVb, d, VIa, b) were subjected to prolonged boiling in an ethanolic solution of an ethanolate or an aqueous solution of sodium sulfide. The low mobility of the halogen atoms in these triazoles can be explained by the assumption that under the action of bases their deprotonation and, as a consequence a decrease in the electrophilicity of the ring, took place.

The UV spectra of the 5-halo-1H-1,2,3-triazoles with the same substituents in position 4 of the ring were practically identical (Table 1). However, the melting point of the iodo-

TABLE 1. Spectral Characteristics of Compounds (I) and (IV-VI)

Compound	IR spectrum (KBr, cm^{-1})				UV spectrum (in water), λ_{max} nm (log ε)	PMR spectrum (in DMSO-D_6), ppm
	C=O	N≡N	C≡N	NH		
Ia	1730[a]	2140[a]	2230[a]			
Ib	1675	2130	2210		247 (3,93)	
Ic	1665	2150	2225		247 (3,98)	8,40 (s, NH), 2,75 (d, J=4,8 Hz., NHMe), 2,72 (s, NMe)
IVa	1715			3540	237 (4,08)	4,47 (2H, q, J=7,2 Hz, CH$_2$), 1,39 (3H, t, J=7,2 Hz, Me)[б]
IVb	1685			3485	231 (3,81)	
IVc	1640			3390	207 (3,84), 237 (3,91)	8,82 (1H, s, NH), 2,86 (3H, d, J=4,8 Hz, NHMe)
IVd	1645				203 (3,97), 258 (4,07)[c]	
Va	1705			3445	237 (3,84)	4,49 (2H, q, J=7,2 Hz, CH$_2$), 1,33 (3H, t, J=7,2 Hz, Me)
Vb	1695			3485	234 (3,72)	
Vc	1650			3400	232 (3,96)	2,83 (3H, d, J=4,8 Hz, NHMe)
Vd	1650				257 (3,95)[c]	
VIa	1730				241 (3,75)	1,37 (3H, t, J=7,3 Hz, Me), 4,48 (2H, q, J=7,3 Hz, CH$_2$)
VIb	1670			3385	218 (3,96), 242 (sh., 3,77)	
VIc	1660			3330	219 (3,94)	2,81 (3H, d, J=4,8 Hz, NHMe), 8,39 (1H, s, NH)
VId	1650				256 (4,08)	

a) In CCl_4.
b) In CD_3OD.
c) In ethanol.

triazole (VIb) differed from that given in the literature [7] for the product synthesized from 5-diazo-1,2,3-triazole-4-carbonamide (X). We reproduced this synthesis and found that the samples of (VIb) which we obtained from the diazoamide (Ib), from the iodotriazole (VIa), and from the diazotriazole (X) were identical in all their physicochemical properties (IR and UV spectroscopy, TLC, mp); a mixture of these samples of (VIb) gave no depression of the melting point.

In contrast to the other hydrogen halides, hydrogen fluoride did not react with the diazonitrile (I) and the corresponding fluorotriazoles (XI) were not formed. Thus, for example, the diazoamide (Ib) remained unchanged in a chloroform solution of hydrogen fluoride at room temperature for a day. Hence, a heterocyclization reaction of carbonyl-substituted diazoacetonitrile derivatives under the action of hydrogen halides has been found, which is a simple and comparatively convenient method of synthesizing 4-carbonyl-substituted 5-halo-1H-1,2,3-triazoles.

EXPERIMENTAL

UV spectra were taken on a Beckman M-26 instrument in water (pH 7) and ethanol, IR spectra were recorded on UR-20 and Specord IR-75 spectrometers in KBr tablets, and also in $CHCl_3$ and CCl_4. PMR spectra were obtained on a Perkin–Elmer R-12-B (60 MHz) instrument in DMSO-D_6 and CD_3OD, with HMDS as internal standard. The course of the reactions was followed and the individuality of the compounds obtained was checked with the aid of TLC on Silufol UV-254 plates in the following solvent systems: chloroform–methanol (9:1) (A); propanol–3 N ammonia (3:1) (B); and butanol–acetic acid–water–ethyl acetate (4:1:1:1) (C). Diazo compounds were revealed by spraying the chromatograms with an ethanolic solution of m-phenylenediamine until the chromatographic spots gave a color reaction. Mass spectra were recorded on MAT-311 instrument under standard conditions; temperature of the source 60°C.*

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

Ethyl 2-Cyano-2-diazoacetate (Ia). With stirring at 0-2°C, a solution of 15.2 g (220 mmole) of $NaNO_2$ in 50 ml of water was added dropwise to a solution of 25.6 g (200 mmole) of

---

*The authors express their gratitude to N. A. Klyuev for recording and interpreting the mass spectra.

TABLE 2. Properties of Compounds (I, IV-VI)

Compound	mp^{a}, °C (from water, decomp.)	$R_f \cdot 10^2$			Found, %				Empirical formula	Calculated, %				Yield, %
		A	B	C	C	H	Cl(Br)	N		C	H	Cl(Br)	N	
Ia									$C_5H_5N_3O_2$					86
Ib	115—116	47	54	74	33,0	2,1		51,0	$C_3H_2N_4O$	32,7	1,8		50,9	78
Ic	118,5—119^{b}	62	59	58	39,1	3,4		45,9	$C_4H_4N_4O$	38,7	3,3		45,5	63
IVa	74—77^{c,d}	85	76	96	34,0	3,3	19,9	23,8	$C_5H_6ClN_3O_2$	34,2	3,4	20,2	23,9	59 (A), 86 (A, B)
IVb	192—194	29	73	86	24,7	1,9	24,2	38,6	$C_3H_3ClN_4O$	24,6	2,1	24,2	38,2	46 (A), 86 (B, C)
IVc	192—193	34	47	88	29,8	3,0	21,9	34,9	$C_4H_5ClN_4O$	29,9	3,1	22,1	34,9	58
IVd	152—153^{c}	80	71		52,4	3,2	16,8	20,5	$C_9H_6ClN_3O$	52,1	2,9	17,1	20,2	88
Va	71—74^{c}	67	81	84	27,4	3,1	36,2	18,9	$C_5H_6BrN_3O_2$	27,3	2,8	36,3	19,1	94
Vb	181—183	65	70	67	18,7	1,8	41,4	29,5	$C_3H_3BrN_4O$	18,9	1,6	41,8	29,3	70 (A), 35 (B)
Vc	184—186	24	77	91	23,4	2,7	39,1	27,7	$C_4H_5BrN_4O$	23,4	2,5	39,0	27,3	67 (A), 60 (B)
Vd	137—138	20	74	95	43,2	2,5	31,6	16,9	$C_9H_6BrN_3O$	42,9	2,4	31,7	16,7	92
VIa	67—68^{c}	75	50	84	22,9	2,6		15,6	$C_5H_6IN_2O_2$	22,5	2,3		15,7	82
VIb	174—176^{d}	73	35	72	15,4	1,3		23,8	$C_3H_3IN_4O$	15,1	1,3		23,5	55 (A), 81 (B), 91 (C)
VIc	182—184	53	40	55	19,4	1,0		22,5	$C_4H_5IN_4O$	19,1	2,0		22,2	65 (A), 93 (B)
VId	184—187^{cd}	17	70	90	30,5	3,5		11,9	$C_9H_6IN_3O \cdot 3H_2O$	30,6	3,4		11,9	45

---

a) The melting points are uncorrected.

b) From ether.

c) Without decomposition. mp 78-81°C [5], 78-79.5°C [6].

d) mp 215°C [7].

e) From ethanol—ether.

the amine (IIa) in 300 ml of 1 N hydrochloric acid. The mixture was kept for 15 min and was then extracted with ether (5 × 200 ml). The extract was dried with Na_2SO_4, and the solvent was evaporated off in vacuum. Reddish oil, unstable in the light. To obtain an analytically pure sample, the diazo ester (Ia) was chromatographed on a column of silica gel (with chloroform as the eluent). Its IR spectrum was identical with that given for the compounds synthesized by diazo-group transfer [2] (Table 1).

2-Cyano-2-diazoacetamide (Ib). With stirring at 0-2°C, a solution of 7.7 g (111 mmole) of $NaNO_2$ in 25 ml of water was added dropwise to a solution of 10 g (101 mmole) of the amine (IIb) in 220 ml of 0.6 N hydrochloric acid. The solution was filtered and was evaporated in vacuum to dryness. The residue was extracted with ether (3 × 50 ml), the extract was evaporated in vacuum to dryness, and the residue was crystallized. Light yellow crystals, reddening in the air. The IR spectra and melting points were identical with those given for the compounds synthesized by diazo-group transfer [2] (Tables 1 and 2).

2-Cyano-2-diazo-N-methylacetamide (Ic). With stirring at a temperature of 0-2°C, a solution of 2.0 g (29 mmole) of $NaNO_2$ in 10 ml of water was added to a solution of 3.0 g (24 mmole) of the amine (IIa) in 40 ml of 1 N hydrochloric acid. The mixture was extracted with ether (8 × 100 ml), and the extract was dried with Na_2SO_4, concentrated in vacuum to a volume of 40 ml, cooled, and filtered. Yellow crystals reddening in the air.

Ethyl 5-Chloro-1H-1,2,3-triazole-4-carboxylate (IVa). A solution of 5.0 g (35.0 mmole) of the diazo ester (Ia) in 30 ml of chloroform was saturated with hydrogen chloride. After 1 day the solvent was evaporated off in vacuum and the residue was crystallized. Colorless acicular crystals.

5-Chloro-1H-1,2,3-triazole-4-carboxamide (IVb). A. A solution of 0.5 g (4.55 mmole) of the diazo amides (Ib) in 100 ml of chloroform was saturated with hydrogen chloride. Then 0.6 g (90%) of the colorless crystalline hydrochloride of 2-cyano-2-diazoacetamide (VIIb) was filtered off. The filtrate was kept at room temperature for 2 months and was crystallized. White microcrystalline powder.

B. The suspension after the passage of hydrogen chloride (see method A) was stirred for 1 day, evaporated in vacuum to dryness, and crystallized.

C. To 7 ml of ethanol that had been saturated with hydrogen chloride was added 0.5 g (4.55 mmole) of the diazoamide (Ic). The suspension was stirred for 30 min, evaporated in vacuum to dryness, and crystallized. The IR spectra and melting points of the products obtained by methods A-C coincided.

5-Chloro-1H-1,2,3-triazole-4-N-methylcarboxamide (IVc) was obtained in a similar manner to the chlorothiazole (IVb) (method C) from the diazoamide (Ic). Reaction time 2 h. Colorless acicular crystals.

4-Benzoyl-5-chloro-1H-1,2,3-triazole (IVd) was obtained in a similar manner to the chlorothiazole (IVb) (method B) from the diazo compound (Id). The time of the reaction was 1 day. Small colorless plates.

Ethyl 5-Bromo-1H-1,2,3-triazole-4-carboxylate (Va) was obtained in a similar manner to the chlorotriazole (IVa) from the diazo ester (Ia) and hydrogen bromide. The reaction time was 1 day. Colorless acicular crystals.

5-Bromo-1H-1,2,3-triazole-4-carboxamide (Vb). A. This was obtained in a similar manner to the chlorotriazole (IVb) (method B) from the diazoamide (Ib) and hydrogen bromide. Reaction time 2 days. Small colorless crystals.

B. A solution of 0.5 g (2.27 mmole) of the ester (Va) in 30 ml of 25% aqueous ammonia was kept in an autoclave at 130°C for 6 h. The water was evaporated off in vacuum, the residue was dissolved in 6 ml of water, and the pH of the solution was brought to 6 with hydrochloric acid. The resulting precipitate was filtered off and crystallized. According to IR spectroscopy and its melting point, the product was identical with that obtained by method A.

5-Bromo-1H-1,2,3-triazole-4-N-methylcarboxamide (Vc). A. This was obtained in a similar manner to the chlorotriazole (IVb) (method B) from the diazoamide (Ic) and hydrogen bromide. Colorless acicular crystals.

B. It was obtained by a method similar to method B for the bromotriazole (Vb) from the ester (Va) and 25% aqueous methylamine. Reaction time 1 h. According to IR and PMR spectroscopy and melting point, the product was identical with the bromotriazole (Vc) obtained by method A.

4-Benzoyl-5-bromo-1H-1,2,3-triazole (Vd) was obtained in a manner similar to method B for the chlorotriazole (IVb) from diazo compound (Id) and hydrogen bromide. Small colorless crystals.

Ethyl 5-Iodo-1H-1,2,3-triazole-4-carboxylate (VIa). A solution of 1.0 g (7.2 mmole) of the diazo ester (Ia) in 30 ml of chloroform was saturated with hydrogen iodide. After 2 days, the solvent was evaporated off in vacuum, and the residue was boiled with water until the bulk of the iodine had been eliminated and was then crystallized. Colorless acicular crystals.

5-Iodo-1H-1,2,3-triazole-4-carboxamide (VIb). A. A solution of 0.5 g (4.55 mmole) of the diazo amide (Ib) in 200 ml of chloroform was saturated with hydrogen iodide. The dihydriodide of 2-cyano-2-diazoacetamine (IXb) was filtered off and was kept in a bottle at 100°C for 12 h. Then 20 ml of water was added, the mixture was boiled to eliminate the bulk of the iodine, and the product was crystallized. Colorless microcrystalline powder.

B. It was obtained in a manner similar to that of method B for the bromotriazole (Vb) from the ester (VIa) and 25% aqueous ammonia. Reaction time 5 h.

C. A solution of 1.84 g (7.24 mmole) of iodine and 2.41 g (14.5 mmole) of KI in 100 ml of water was treated with 1 g (7.24 mmole) of the diazotriazole (X) and the mixture was kept at 90°C for 1 h. Then the solvent was evaporated off in vacuum to dryness and the residue was crystallized. According to IR and UV spectroscopy, and also its melting point, the product was identical with the iodotriazole (VIb) obtained by methods A and B. A mixture of the products gave no depression of the melting point.

5-Iodo-1H-1,2,3-triazole-4-N-methylcarboxamide (VIc). A. This was obtained in a manner similar to method A for the iodotriazole (VIb) from the diazoamide (Ib) and hydrogen iodide. Reaction time 2 h. Colorless acicular crystals.

B. This was obtained in a manner similar to method B for the bromotriazole (Vb) from the ester (Va) and 25% aqueous methylamine. Reaction time 2 h. According to IR and PMR spectroscopy and its melting point the product was identical with that obtained by method A.

4-Benzoyl-5-iodo-1,2,3-triazole trihydrate (VId) was obtained in a similar manner to the iodotriazole (VIa) from diazo compound (Id) and hydrogen iodide. Reaction time 1 day. Colorless prisms.

LITERATURE CITED

1. M. Nakai, K. Harada, and Y. Mori, US Patent No. 4,269,982, Chem. Abstr., 95, 62231 (1980).
2. H. Balli, R. Löw, V. Müller, H. Rempfler, and A. Sezen-Gezgin, Helv. Chim. Acta, 61, 97 (1978).
3. E. Ciganek, J. Org. Chem., 30, 4198 (1965).
4. Yu. M. Shafran, V. A. Bakulev, V. S. Mokrushin, and Z. V. Pushkareva, Khim. Geterosikl. Soedin., No. 12, 1697 (1982).
5. D. R. Buckle and C. J. Rockell, J. Chem. Soc., Perkin Trans. I, No. 2, 627 (1982).
6. M. P. Nemeryuk, A. L. Sedov, I. Krzhpelka, Ya. Benesh, and T. S. Safonova, Khim. Geterotsikl. Soedin., No. 10, 1398 (1983).
7. Y. F. Shealy and C. A. O'Dell, J. Med. Chem., 9, 733 (1966).

SYNTHESIS AND PROPERTIES OF AZOLES AND THEIR DERIVATIVES.

36.* SYNTHESIS OF 2-AMINO-1,3,4-OXADIAZOLES, 2-AMINO-1,3,4-THIADIAZOLES, AND 1,2,4-TRIAZOLINE-3-THIONES CONTAINING INDOLYL RADICALS

V. I. Kelarev, G. A. Shvekhgeimer,
and A. F. Lunin

UDC 547.752'793.3:542.953.2:
543.422.4

On the heterocyclization of 1-(indol-3-ylcarbonyl)thiosemicarbazides, depending on the conditions of performing the reaction, either 1,2,4-triazoline-3-thiones, 2-amino-1,3,4-thiadiazoles, or 2-amino-1,3,4-oxadiazoles containing an indolyl residue in position 5 are obtained. 1,2,4-Triazoline-3-thiones and 2-amino-1,3,4-thiadazoles have also been synthesized by the reaction of the hydrochloride of ethyl indol-3-carboximidate with thiosemicarbazides.

Continuing an investigation of the synthesis of indolylazoles [1-4], in the present paper we report the preparation of 2-amino-1,3,4-oxadiazoles, 2-amino-1,3,4-thiadiazoles, and 1,2,4-triazoline-3-thiones each containing an indolyl residue. There has been only limited information concerning bisheterocyclic compounds of this type in the literature hitherto [5, 6].

It is known [7, 8] that the starting materials for the synthesis of amino and mercapto derivatives of 1,3,4-oxadiazoles, 1,3,4-thiadiazoles, and 1,2,4-triazoles may be compounds containing a thiosemicarbazide fragment. In the present work, as the initial compound we used the 1-(indol-3-ylcarbonyl)thiosemicarbazides (IIa, b) which are readily formed from indole-3-carbohydrazide (I).

---

*For communication 35, see [1].

I. M. Gubkin Moscow Institute of the Petrochemical and Gas Industries. Translated from Khimiya Geterotsilicheskikh Soedinenii, No. 9, pp. 1271-1276, September, 1984. Original article submitted January 21, 1984.