ETHYL 4-THIOCYANATO-3-OXO-2-ARYLHYDRAZONO-1-BUTANOATES IN HETEROCYCLIZATION REACTIONS.

2.* SYNTHESIS AND STRUCTURE OF 2-IMINO-5-[1-(ARYLHYDRAZONO)-2-ETHOXYOXALYL]-4,5-DEHYDRO-1,3-OXATHIOLANES AND 2-CHLORO-4-[1-(ARYLHYDRAZONO)-2-ETHOXYOXALYL]-1,3-THIAZOLES

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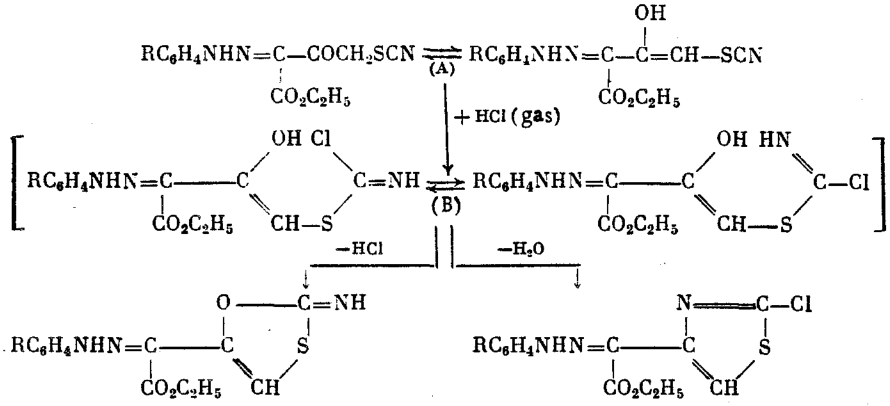
Thiocyanates and α-keto thiocyanates are reactive substances [1], and many oxazothiazoline [2], 2-chlorothiazole [3], and 2-chloro-1,3-benzothiazinone [4] heterocyclic systems have been synthesized from them.

We have previously obtained new substituted ethyl 4-thiocyanato-3-oxo-2-arylhydrazono-1-butanoates [5] and studied their reaction with gaseous HCl in benzene [6]. Continuing these investigations, we have established that the formation of the final products of this reaction (see the scheme) depends substantially on the nature of the R substituent in the phenyl ring.



(I)—(VI) (VII)—(IX)

Thus, only 2-imino-5-[1-(phenyl(2-methoxyphenyl, 4-methoxyphenyl)hydrazono)-2-ethoxyoxalyl[-4,5-dehydro-1,3-oxathiolanes (I), (IV), and (V) are formed in the case of the electron-donor methoxy group and hydrogen. When electron-acceptor substituents are present in the phenyl ring (R = o-Cl, p-Cl, m-CF_3), 2-chloro-4-[1-(arylhydrazono)-2-ethoxyoxalyl]-1,3-thiazoles (VII)-(IX) are obtained in addition to substituted 1,3-oxathiolanes (II), (III), and (VI). The structures and properties of the compounds obtained — substituted 1,3-oxathiolanes (I)-(VI) and 2-chloro-1,3-thiazoles (VII)-(IX) — were proved by the PMR, IR, and mass spectra, as well as by the results of elementary analysis. Data from x-ray diffraction analysis were obtained for (V) and (IX).

The data obtained make it possible to state an assumption regarding the way in which the reaction proceeds. Ethyl 4-thiocyanato-3-oxo-2-arylhydrazono-1-butanoates react with HCl in absolute benzene in tautomeric form A. In the first step HCl adds to the polarized $-S-\overset{\delta+}{C}\equiv\overset{\delta-}{N}$ bond (B). Either substituted 1,3-oxathiolanes or 2-chloro-1,3-thiazoles or both products are then formed, depending on the donor-acceptor nature of the R substituent in the phenyl ring. Cleavage of the O—H and C—Cl bonds and splitting out of HCl with the for-

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*For previous communication, see [6].

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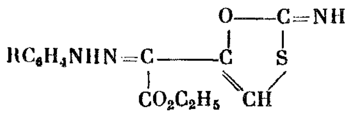
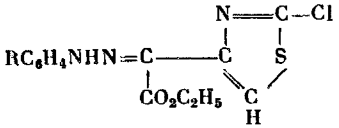
TABLE 1. 2-Imino-5-[1-(arylhydrazono)-2-ethoxyoxalyl]-4,5-dehydro-1,3-oxathiolanes



Compound	R	Yield, %	Mp, °C	Found, %				Empirical formula	Calc., %			
				C	H	N	S		C	H	N	S
(I)	H	80	215	53,27 53,28	4,59 4,62	14,40 14,41	11,22 11,27	$C_{13}H_{13}N_3O_3S$	53,59	4,49	14,42	11,00
(II)	*o*-Cl *	50	225	47,44 47,56	4,09 4,18	12,81 13,00	9,72 9,60	$C_{13}H_{12}ClN_3O_3S$	47,89	3,70	12,89	9,84
(III)	*p*-Cl **	70	232	47,80 47,77	3,63 3,64	12,68 12,83	9,67 9,80	$C_{13}H_{12}ClN_3O_3S$	47,89	3,70	12,89	9,84
(IV)	*o*-OCH_3	62	221	52,22 52,25	4,54 4,67	13,33 13,00	9,86 10,02	$C_{14}H_{15}N_3O_4S$	52,32	4,74	13,07	9,97
(V)	*p*-OCH_3	59	217	52,75 52,73	4,62 4,66	12,82 12,96	10,10 10,21	$C_{14}H_{15}N_3O_4S$	52,32	4,74	13,07	9,97
(VI	*m*-Cl_3 ***	42	205	46,88 46,84	3,58 3,67	11,50 11,34	9,01 9,17	$C_{14}H_{12}F_3N_3O_3S$	46,79	3,37	11,69	8,90

*Found, %: Cl 11.03; 11.11. Calculated, %: Cl 10.88.
**Found, %: Cl 11.01; 10.88. Calculated, %: Cl 10.88.
***Found, %: F 15.54; 15.73. Calculated, %: F 15.86.

TABLE 2. 2-chloro-4-[1-(arylhydrazono)-2-ethoxyoxalyl]-1,3-thiazoles



Compound	R	Yield, %	Mp, °C	Found, %					Empirical formula	Calc., %				
				C	H	Cl	N	S		C	H	Cl	N	S
(VII)	*o*-Cl	40	142	44,92 45,05	3,34 3,55	20,35 20,54	11,98 11,81	9,43 9,54	$C_{13}H_{11}Cl_2N_3O_2S$	45,36	3,22	20,60	12,20	9,31
(VIII)	*p*-Cl	25	122	44,90 45,10	3,00 3,19	20,51 20,64	11,98 12,11	8,90 9,21	$C_{13}H_{11}Cl_2N_3O_2S$	45,36	3,22	20,60	12,20	9,31
(IX)	*m*-CF_3*	15	108	44,64 44,77	2,92 2,95	9,40 9,37	12,22 12,32	8,12 8,25	$C_{14}H_{11}F_3ClN_3O_2S$	44,50	2,93	9,38	11,12	8,48

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*Found, %: F 15.18; 15.22. Calculated, %: F 15.08.

mation of a new O–C bond and the production of the oxathiolane hetero ring occur in the case R = H, o-OCH_3, p-OCH_3. Two reaction pathways are possible in the case R = Cl, CF_3. In the case of splitting out of HCl the reaction proceeds via the pathway described above and leads to the formation of oxathiolane derivatives (II), (III), and (VI). In addition to this, cleavage of the C–OH and N–H bonds, the formation of a molecule of water, and the formation of a ring involving the C–N bond to give substituted 2-chloro-1,3-thiazoles (VII)-(IX) may occur; the yields of oxathiolane derivatives are higher in this case than the yields of thiazole derivatives (Tables 1 and 2).

EXPERIMENTAL

The PMR spectra were recorded with a Bruker WP-200 spectrometer with an operating frequency of 200 MHz. The molecular weights were determined with an MS-1302 mass spectrograph. The IR spectra of KBr pellets of the compounds were measured with a UR-20 automatic double-beam spectrometer; the spectra at 400-700 cm^{-1} were recorded with a KBr prism, the spectra at 700-1800 cm^{-1} were recorded with an NaCl prism, and the spectra at 1800-4000 cm^{-1} were recorded with an LiF prism. The x-ray diffraction study of (V) and (IX) was carried out with an RÉD-4 automatic four-circle diffractometer in CuK_α and MoK_α emissions, respectively, with a graphite monochromator by the method of $\omega/2\theta$ scanning. The structures were determined by the direct method and refined by the method of least squares within anisotropic (for the Cl, S, F, O, N, and C atoms), isotropic (for the H atoms), and block-diagonal approximations using the Cruikshank weight scheme up to R = 0.057 (V) and 0.095 (IX). Pictures of the molecules were obtained by means of the program in [7]. All of the calculations were made with a BÉSM-6 computer by means of the set of Rentgen-75 programs [8].

2-Imino-5-[1-(phenylhydrazono)-2-ethoxyoxalyl]-4,5-dehydro-1,3-oxathiolane (I). A solution of 2.9 g (0.009 mole) of ethyl 4-thiocyanato-3-oxo-2-phenylhydrazono-1-butanoate in 100 ml of absolute benzene was cooled to 5-10°C, and dry HCl was then passed into the mixture for 6 h. The mixture was then allowed to stand at ~20°C for 1 day, and the resulting precipitate was filtered, washed twice with absolute benzene, and dried. The precipitate was dissolved in 100 ml of absolute alcohol, and the solution was refluxed for 4 h. The resulting precipitate was filtered, washed with absolute alcohol, and crystallized twice from freshly distilled DMF. The yield was 2.4 g. Mass spectrum (m/z): M^+ 291 (calculated value 291). PMR spectrum [$(CD_3)_2CO$, δ, ppm)]: 7.52 (C_6H_5), 6.95 (C–H proton of the 1,3-oxathiolane ring), 11.17 (=N–H), 11.95 (NH–N=), 4.31 (CH_2), 1.30 (CH_3). IR spectrum (ν, cm^{-1}): 3240, 3200, 3180, 3310 (N–H), 2980, 2940, 2870 (CH_3, CH_2, CH), 1600 (C=O), 1600 (C=N), 1540 (C_6H_5).

2-Imino-5-[1-(2-chlorophenylhydrazono)-2-ethoxyoxalyl]-4,5-dehydro-1,3-oxathiolane (II). This compound was similarly obtained. Mass spectrum (m/z): M^+ 325 (calculated value 325). PMR spectrum (DMSO-d_6, δ, ppm): 7.30 (C_6H_5), 6.83 (C–H proton of the 1,3-oxathiolane ring), 11.28 (=N–H), 12.47 (NH–N=), 4.33 (CH_2), 1.31 (CH_3). IR spectrum (ν, cm^{-1}): 3340, 3220, 3170, 3120 (N–H), 2990, 2980, 2960 (CH_3, CH_2, CH), 1660 (C=O), 1590 (C=N), 1530 (C_6H_4).

2-Imino-5-[1-(4-chlorophenylhydrazono)-2-ethoxyoxalyl]-4,5-dehydro-1,3-oxathiolane (III). This compound was similarly obtained. PMR spectrum (DMSO-d_6, δ, ppm): 7.43 (C_6H_4), 6.69 (C–H proton of the 1,3-oxathiolane ring), 11.22 (=N–H), 11.84 (NH–N=), 4.31 (CH_2), 1.30 (CH_3). IR spectrum (ν, cm^{-1}): 3360 (N–H), 2990, 2950, 2910 (CH_3, CH_2, CH), 1710 (C=O), 1560 (C=N), 1500-1600 (C_6H_4).

2-Imino-5-[1-(2-methoxyphenylhydrazono)-2-ethoxyoxalyl]-4,5-dehydro-1,3-oxathiolane (IV). This compound was similarly obtained. PMR spectrum (DMSO-d_6, δ, ppm): 6.97 (C_6H_4), 6.70 (C–H proton of the 1,3-oxathiolane ring), 11.15 (=N–H), 12.36 (NH–N=), 4.31 (CH_2), 3.83 (OCH_3), 1.30 (CH_3). IR spectrum (ν, cm^{-1}): 3350, 3300, 3280, 3170 (N–H), 2950, 2930, 2820 (CH_3–), CH_2–, CH–), 1670 (C=O), 1540 (C=N), 1500-1600 (C_6H_4).

2-Imino-5-[1-(4-methoxyphenylhydrazono)-2-ethoxyoxalyl]-4,5-dehydro-1,3-oxathiolane (V). This compound was similarly obtained. Mass spectrum (m/z): M^+ 321 (calculated value 321). PMR spectrum ($CDCl_3$, δ, ppm): 6.86 (C_6H_4), 11.10 (=N–H), 12.07 (NH–N=), 6.61 (C–H proton of the 1,3-oxathiolane ring), 4.29 (CH_2), 3.68 (OCH_3), 1.29 (CH_3). IR spectrum (ν, cm^{-1}): 3310, 3250, 3200, 3170 (N–H), 2980, 2940, 2840 (CH_3, CH_2, CH), 1660 (C=O), 1610 (C=N), 1500-1600 (C_6H_4).

X-ray Diffraction Analysis. Compound (V) crystallized in the form of yellow triclinic prisms. The principal crystallographic data are as follows: molecular weight 321.36, a = 9.012(2), b = 11.742(2), c = 8.510(2) Å, α = 92.24(2)°, β = 62.80(1)°, γ = 105.68(1)°, V =

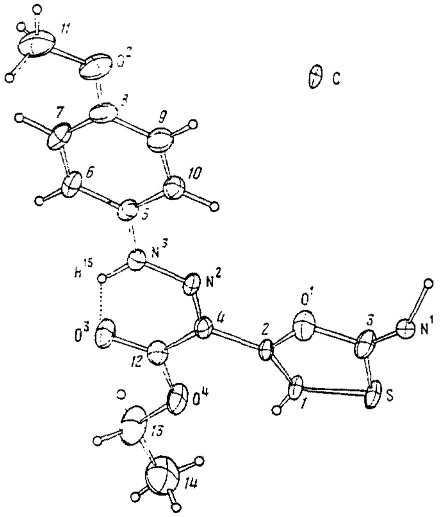

Fig. 1. General form and designation of the atoms of the (V) molecule.

767.4(2) Å^3, d_{calc} = 1.39 g/cm^3, Z = 2, space group $P\bar{1}$. The intensities of 1416 independent nonzero [$I > 3\sigma(I)$] reflections were measured over the range $3.9° \le \theta = 53.8°$. Absorption was disregarded [$\mu(CuK_\alpha) = 20.2\ cm^{-1}$]. The general form of the molecule is shown in Fig. 1. The syn-S-cis form of the hydrazone fragment stabilized by an N—H...O intramolecular hydrogen bond with the following parameters is realized in the molecule: $O^3...H^{15}$ 1.880(2) Å, H^{15}—N^3 0.95(3) Å, $O^3...N^3$ 2.617(3) Å, angle $N^3H^{15}O^3$ 132(4)°. The lengths of the N^2—N^3 [1.325(4) Å] and N^2=C^4 [1.310(4) Å] bonds are virtually equalized; according to the Hafelinger calculations from [9], this constitutes evidence for a significant degree of participation of the unshared pair of the amino N atom in conjugation, which is in agreement with data from their IR spectra. In the planar oxathiolane ring the lengths of the bonds of the two heteroatoms with the carbon atoms are not equivalent: S—C^1 1.735(3) Å and S—C^3 1.770(3) Å, O^1—C^3 1.364(5) Å, and O^1—C^2 1.404(3) Å. The observed difference cannot be explained by different real states of hybridization of the carbon atoms that participate in the bonds, since the bond of the same C^3 atom with the O^1 atom is shortened, whereas that with the S atom is lengthened. The crystal structure of (V) is the result of packing of discrete molecules with normal Van der Waals contacts.

2-Imino-5-[1-(3-trifluoromethylphenylhydrazono)-2-ethoxyoxalyl]-1,3-oxathiolane (VI). This compound was similarly obtained. PMR spectrum (DMSO-d_6, δ, ppm): 7.98 (C_6H_4), 6.78 (C—H proton of the 1,3-oxathiolane ring), 11.45 (=N—H), 11.85 (NH—N=), 4.38 (CH_2), 1.35 (CH_3). IR spectrum (ν, cm^{-1}): 3340, 3240, 3190, 3120 (N—H), 2940, 2920, 2920 (CH_3, CH_2, CH), 1650 (C=O), 1560 (C=N), 1500-1600 (C_6H_4).

2-Chloro-4-[1-(2-chlorophenylhydrazono)-2-ethoxyoxalyl]-1,3-thiazole (VII). This compound was obtained from the mother liquor from the preparation of (II). The filtrate was evaporated in vacuo, and the residue began to crystallize after 10 h. The product was crystallized twice from alcohol. The yield was 0.8 g. Mass spectrum (m/z): M^+ 344 (calculated value 344). PMR spectrum [$(CD_3)_2CO$, δ, ppm]: 6.98 (C_6H_4), 8.42 (C—H proton of the methylidyne group), 12.88 (NH—N=), 4.26 (CH_2), 1.29 (CH_3). IR spectrum (ν, cm^{-1}): 3290, 3100 (N—H), 3015 (CH_3, CH_2, CH), 1700 (C=O), 1610 (C=N), 1490-1560 (C_6H_4), 790, 750, 730 (C—Cl).

2-Chloro-4-[1-(4-chlorophenylhydrazono)-1,3-thiazole (VIII). This compound was obtained from the mother liquor from the preparation of (III). The filtrate was evaporated in vacuo, and the residue began to crystallize after 1 h. The product was crystallized twice from alcohol. The yield was 0.5 g. Mass spectrum (m/z): M^+ 344 (calculated value 344). PMR spectrum (DMSO-d_6, δ, ppm): 7.28 (C_6H_4), 8.18 (C—H proton of the thiazole ring), 11.62 (NH—N=), 4.22 (CH_2), 1.26 (CH_3). IR spectrum (ν, cm^{-1}): 3215, 3185 (N—H), 3005, 2980, 2960, 2920 (CH_3, CH_2, CH), 1710 (C=O), 1630, 1610 (C=N), 1565, 1510 (C_6H_4), 790, 760, 720 (C—Cl).

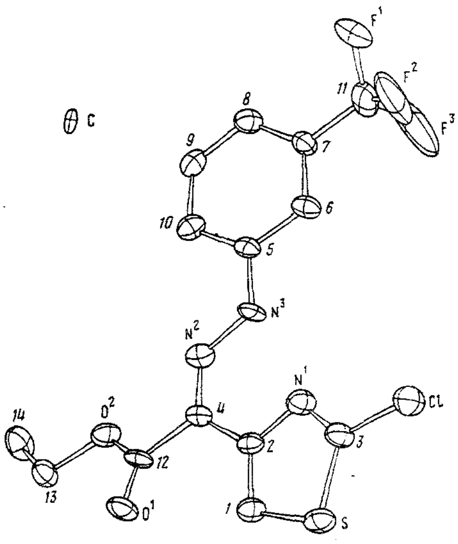

Fig. 2. General form and designation of the atoms of the (IX) molecule.

2-Chloro-4-[1-(3-trifluoromethylhydrazono)-2-ethoxyoxalyl)-1,3-thiazole (IX). This compound was obtained from the mother liquor from the preparation of (VI). The filtrate was evaporated in vacuo, and the residue began to crystallize after 1 h. The product was crystallized from alcohol. The yield was 0.2 g. PMR spectrum (DMSO-d_6, δ, ppm): 7.35 (C_6H_4), 8.17 (C—H proton of the thiazole ring), 11.54 (NH—N=), 4.22 (CH_2), 1.26 (CH_3). IR spectrum (ν, cm^{-1}): 3215, 3190 (N—H), 3010, 2990, 2960, 2920 (CH_3, CH_2, CH), 1715 (C=O), 1630, 1610 (C=N), 1550, 1510 (C_6H_4), 790, 710 (C—Cl).

X-ray Diffraction Analysis. Compound (IX) crystallized in the form of light-yellow monoclinic plates. The principal crystallographic data are as follows: molecular weight 377.77, a = 10.907(4), b = 8.120(3), c = 18.680(7) Å, γ = 90.52(2)°, V = 1654.3(5) $Å^3$, d_{calc} = 1.52 g/cm^3, Z = 4, space group $P2_1/c$. The intensities of 1172 independent nonzero ($I_0 > 3\sigma$ (I)] reflections were measured over the range $1.9° \le \theta \le 32.1°$. Absorption was disregarded [$\mu(MoK_\alpha) = 4.0\ cm^{-1}$]. The general form of the (IX) molecule is shown in Fig. 2, from which it is apparent that the anti-S-trans form of the hydrazone fragment stabilized by the formation of an intramolecular hydrogen bond of the N—H...N type with an $N^1...N^3$ distance of 2.71(1) Å is realized in the molecule. The planar (within the limits ±0.02 Å) 1,3-thiazole hetero ring is characterized by the following interatomic distances: S—C^1 1.71(1), S—C^3 1.72(1), N^1—C^2 1.37(1), N^1—C^3 1.27(1), C^1—C^2 1.34(1) Å.

CONCLUSIONS

Substituted 1,3-oxathiolanes or substituted 2-chloro-1,3-thiazoles are formed in the reaction of ethyl 4-thiocyanato-3-oxo-2-arylhydrazono-1-butanoates with gaseous HCl in absolute benzene, depending on the electron-donor properties of the substituents in the arylhydrazone.

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