REACTION OF ARENEDIAZONIUM SALTS WITH RHODANINE, THIOHYDANTOIN, AND THEIR DERIVATIVES

E. P. Nesynov, M. M. Besprozvannaya, and P. S. Pel'kis

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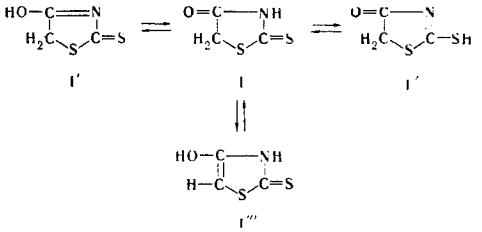
Under conditions of the O,S-arylation of rhodanine and isorhodanine by arenediazonium salts, 5-arylhydrazono-2-arylthio-2-thiazolin-4-ones and 5-arylhydrazono-4-arylthio-3-thiazolin-2-ones have been obtained. Under similar conditions, 5-ethylrhodanine forms not only 2-arylthio-5-ethyl-2-thiazolin-4-ones but also 2-arylazothio-5-ethyl-2-thiazolin-4-ones.

It has been shown [1, 2], for the case of monothiobarbituric acid and β-thioxo compounds containing an imino group in the α position, that in the arylation with arenediazonium salts of substances containing active methylene, amide, and thioamide groups the reaction takes place firstly at the methylene group, then at the thioamide group, and finally at the amide group. On the basis of the investigations performed [1-5] it has been concluded that S-arylation is possible for compounds capable of thioamide–thioimidic acid tautomerism.

The aim of the present work was to continue the study of the O,S-arylation reaction for the case of rhodanine (I), its 5-ethyl derivative (II), and isorhodanine (III). These compounds tend to thioamide–thioimidic acid tautomerism, which makes it possible to assume arylation by arenediazonium salts at the sulfur atom of the thioamide group.

Three types of tautomerism are possible for (I): amide–imidic acid (I ⇄ I'), thioamide–thioimidic acid (I ⇄ I"), and keto–enol (I ⇄ I'").



Amide–imidic acid tautomerism has not been shown experimentally and it is less likely than keto–enol tautomerism in view of the fact that thioamide–thioimidic acid tautomerism is realized for (I).

The coupling of arenediazonium salts with (I) in an ethanolic medium or in the presence of pyridine leads to 5-arylazo-2-thioxothiazolidin-4-ones (azorhodanines) (IV) [6-8].

With arenediazonium salts, isorhodanine (III) reacts similarly to (I), forming 5-arylazo-4-thioxothiazolidin-2-ones (V) [8].

We have established that under the conditions of the O,S-arylation reaction of (I-III), the reaction of the arenediazonium cation takes place at the sulfur atom with the formation of, respectively, 5-arylazo-2-arylthio-2-thiazolin-4-ones (VIa-c); 2-arylthio-5-ethyl-2-thiazolin-4-ones (VIIa-e), and 2-arylazothio-5-ethyl-2-thiazolin-4-ones (VIIIa-d); and 5-arylazo-4-arylthio-3-thiazolin-2-ones (IXa, b).

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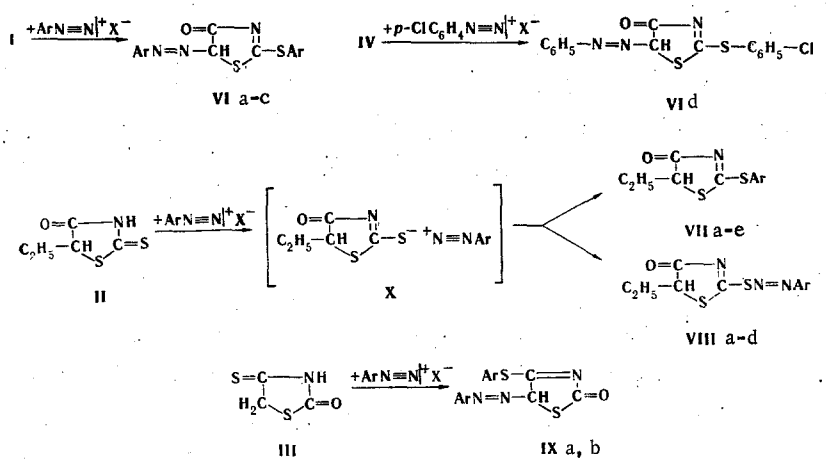
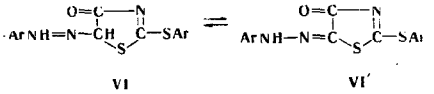


VIa, VIIa, IXa Ar=C_6H_5; VIb, VIIb, IXb, Ar=p-ClC_6H_4; VIc, VIIIb Ar=p-$CH_3C_6H_4$; VIIIa Ar=m-$CH_3C_6H_4$; VIIc, Ar=m-$O_2NC_6H_4$; VIId Ar=p-$O_2NC_6H_4$; VIIe Ar=o-CH_3O, p-$O_2NC_6H_3$; VIIIc Ar=p-$CH_3OC_6H_4$; VIIId Ar=p-BrC_6H_4

The reaction of (I) or (III) with an arenediazonium salt is accompanied by the reaction of the arenediazonium cation at the active methylene group, and therefore it is impossible to isolate the products of S-arylation alone – the 2-arylthio-2-thiazolin-4-one or the 4-arylthio-3-thiazolin-2-one, respectively.

In none of the cases of the arylation of (I-IV) was it possible to obtain O-arylated or O,S-diarylated derivatives of 2- or 3-thiazoline or their O-aryl-S-arylazo-substituted derivatives, in spite of the fact that the arenediazonium salts were used in excess in the reaction. It is obvious that the methylene group in (I) and (III) is more reactive than the thioamide and amide groups. Apparently, compounds (I) and (III) are CH acids (pK_a value for (I) 6.9 [9], see also [10]). Furthermore, according to the literature [6-8] for (VIa-d) it is possible to assume the existence of hydrazone–azo tautomerism (VI $\rightleftarrows$ VI'), because of which no keto–enol tautomerism (I $\rightleftarrows$ I''') takes place and no O-arylation products are formed.



The structures of compounds (VIa-d), (VIIIa-e), and (IXa, b) were shown by alkaline and acid hydrolysis and also by ammonolysis and hydrazinolysis. This gave the corresponding thiophenols and diaryl disulfides, which shows arylation at the sulfur atom. No phenols were found among the reaction products. In addition, (VIa) was obtained independently – by the arylation of (IV) with the corresponding arenediazonium salt under similar conditions (yield 40%).

In the reaction of compound (II) with arenediazonium salts, the formation of (VIIa-e) was accompanied by an ionic–covalent rearrangement of the intermediate arenediazonium 5-ethyl-4-oxo-2-thiazolin-2-yl sulfide (X), which competes with its decomposition. It was impossible to isolate (X) in the free state. However, if 5-10 min after the beginning of the reaction the (yellow) precipitate that had formed was separated off, it was possible to show qualitatively the properties characteristic of a diazonium salt (coupling with β-naphthol, instability on heating above 5-10°C, etc.). At room temperature, the precipitate decomposed with the liberation of nitrogen and the formation of (VII) or (VIII) depending on the substituents in the arene nucleus. The formation of similar diazonium salts and of arylazo sulfides analogous to (VIII) has been reported for the case of the arylation of 2-mercaptobenzazoles with arenediazonium salts [2, 3].

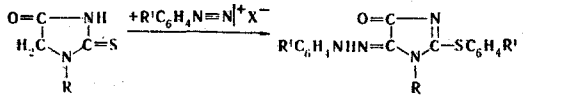
The reaction of (II) with arenediazonium salts containing electropositive substituents in the arene nucleus gave (VIIIa-d) (Table 3). In this case, the ionic–covalent rearrangement (X) → (VIIIa-d) takes place. However, the use in the reaction of arenediazonium salts with electronegative substituents in the aryl nucleus favors the homolytic decomposition (X) → (VIIa-e) with the liberation of nitrogen and the formation of the sulfides (VIIa-e) (Table 2).

On analyzing the formation of the 2-arylazothiobenzazoles (XI) [2, 3] and (VIIIa-d), it may be concluded that the hetero chain –S–N=N– transmits electronic influences between the aromatic nucleus Ar and the thiazole ring. The latter also possesses electronic mobility. Consequently, the strength of the S–N bond is determined by these factors and by the nature of the substituents in (XI) and (VIII). The displacement of the electrons of the thiazole ring in the direction of the benzene nucleus of benzothiazole and of the p-electrons of the α- and β-nitrogen atoms of the arylazo group in the direction of the electronega-

tive substituent in the aryl nucleus strengthens the S–N bond in (XI), while an electropositive substituent weakens this bond. The presence in position 5 of the thiazoline ring of an electropositive alkyl group causes the opposite action of the substituent in the aryl nucleus of (VIII) on the strength of the S–N bond. Apparently, such electronic effects take place even at the stage of the formation of (X) and explain the occurrence of the ionic–covalent rearrangement (X) → (VIII) or that of the homolytic decomposition (X) → (VII).

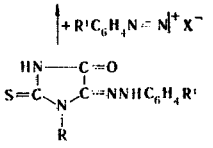
No reaction of the arenediazonium cation at the methine group of (II) takes place, and the expected 5-arylazo-2-arylthio-5-ethyl-2-thiazolin-4-ones are not formed.

The replacement of the sulfur heteroatom in (I) by an imino group leads to a decrease in the reactivity of the methylene group under the conditions of the O,S-arylation reaction, which is in harmony with the literature [11]. It has been found that thiohydantoin (XII) and 1-acetylthiohydantoin (XIII), on reaction with arenediazonium salts, form the corresponding arylthio derivatives of 2-imidazolin-4-one (XIVa-c), which may also be obtained from the thiohydantoin 5-arylhydrazones (XVa, b):



XII, XIII

XIV a-c



XVa, b

a R = R' = H;
b R = CH_3CO, R' = H;
c R = CH_3CO, R' = *p*-CH_3O

The structure of (XIVa-c) was confirmed by the results of acid and alkaline hydrolysis and hydrazinolysis, as has been shown also for (VIa-d).

We express our thanks to S. N. Baranov for providing samples of (I) and (III) and for his interest in the investigation.

EXPERIMENTAL

5-Arylazo-2-arylthio-2-thiazolin-4-ones (VIa-d). A solution of 0.5 g (0.0038 mole) of rhodanine in 100 ml of acetone was treated with 1.5 ml of 10% caustic soda. After 1 h, 3 g of sodium acetate in 10 ml of water was added to the solution, the mixture was cooled to 0°C and, slowly, with stirring, a solution of the arenediazonium salt was added (diazotization was performed with 0.0076 mole of the arylamine, 10 ml of water, 2 ml of concentrated hydrochloric acid, 0.52 g of sodium nitrite in 5 ml of water, and 5 g of ice; diazotization time 1 h). After 16 h, the precipitate that had deposited was filtered off and dried. Then it was dissolved in 30 ml of benzene, the insoluble residue was filtered off, and the filtrate was chromatographed on alumina (height of the layer 6 cm, diameter 1 cm). The second zone (brown) was collected and its solution was diluted twofold with benzene, and a threefold amount of petroleum ether (fraction with bp 70-100°C) was added. After 3 h the precipitate that had deposited was filtered off. The filtrate was evaporated, and the residue was dried to constant weight, giving (VIa-c) (see Table 1).

The second method of obtaining (VIa), and also (VId), was similar to the above-described synthesis of (VIa-c) but instead of rhodanine (I) the corresponding 5-arylazo-2-thioxothiazolidin-4-ones (IV) and aryldiazonium salts were used in the reaction in equimolecular amounts.

TABLE 1. Arylthio Derivatives of 5-Arylazothiazolinones (VIa-d, IXa, b)

Compound	mp, °C	Empirical formula	Found, %		Calc., %		Yield, %
			N	S	N	S	
VIa*	92–91	$C_{15}H_{11}N_3OS_2$	13,0	20,1	13,1	20,1	25
VIb	194	$C_{15}H_9Cl_2N_3OS_2$	11,0	17,0	11,0	16,8	10
VIc	172	$C_{17}H_{15}N_3OS_2$		19,0		18,8	9
VId	195	$C_{15}H_{10}ClN_3OS_2$		18,7		18,1	20
IXa	87–89 (dec.)	$C_{15}H_{11}N_3OS_2$	13,1	–	13,1	–	50
IXb	74–75 (dec.)	$C_{15}H_9Cl_2N_3OS_2$	10,6	17,0	11,0	16,8	50

* Found: C 57.8, H 3.7%. Calculated: C 57.5; H 3.5%.

TABLE 2. 2-Arylthio-5-ethyl-2-thiazolin-4-ones (VIIa-e)

Compound	mp, °C	Empirical formula	S, %		Yield, %
			found	calc.	
VIIa	84—85	$C_{11}H_{11}NOS_2$	27,3	27,0	62
VIIb	80—82	$C_{11}H_{10}ClNOS_2$	23,5	23,6	85
VIIc	Viscous oil	$C_{11}H_{10}N_2O_3S_2$	22,4	22,7	50
VIId*	46—47	$C_{11}H_{10}N_2O_3S_2$	22,7	22,7	52
VIIe	27—28	$C_{12}H_{12}N_2O_4S_2$	20,4	20,5	50

*Found: C 46.8; H 4.1; N 10.2%. Calculated: C 46.8; H 3.6; N 9.9%.

TABLE 3. 2-Arylazothio-5-ethyl-2-thiazolin-4-ones (VIIIa-d)

Compound	Decomp. pt., °C	Empirical formula	Found, %		Calc., %		Yield, %
			N	S	N	S	
VIIIa	79—80	$C_{12}H_{13}N_3OS_2$	—	22,6	—	22,9	65
VIIIb	81—82	$C_{12}H_{13}N_3OS_2$	15,1	22,8	15,1	23,0	67
VIIIc	83—84	$C_{12}H_{13}N_3O_2S_2$	—	21,3	—	21,6	55
VIIId	105—106	$C_{11}H_{10}BrN_3OS_2$	12,3	18,4	12,2	18,6	50

Compounds (VIa-d) are crystalline substances soluble in acetone, dioxane, and benzene, sparingly soluble in petroleum ether, and insoluble in water.

5-Arylazo-4-arylthio-3-thiazolin-2-ones (IXa, b). A solution of 0.8 g of caustic soda in 3 ml of water was added to a solution of 1.33 g (0.01 mole) of isorhodanine in 200 ml of acetone. After 1 h, 9.5 g of sodium acetate in 50 ml of water was added to the resulting solution, the mixture was cooled to 0°C, and a solution of the arenediazonium salt was slowly added (diazotization was performed with 0.02 mole of the arylamine, 4.5 ml of concentrated hydrochloric acid, 1.26 g of sodium nitrite, and 10 g of ice; the diazotization time was 1 h). After 16 h, the acetone was evaporated off from the mixture. The precipitate that deposited was filtered off, 25 ml of water was added, and the mixture was extracted with 150 ml of diethyl ether. The ether was evaporated off, and the residue was dissolved in 50 ml of benzene and chromatographed as described for (VIa-c), giving (IXa). In the isolation of (IXb), the benzene solution after chromatography was evaporated in vacuum to dryness, i.e., precipitation with petroleum ether was not used.

Compounds (IXa and b) (Table 1) are soluble in benzene, acetone, and dioxane and less soluble in petroleum ether. Their melting points are lower than those of (VIa-d).

2-Arylthio-5-ethyl-2-thiazolin-4-ones (VIIa-e). A solution of 0.5 g (0.003 mole) of 5-ethylrhodanine (II) in 50 ml of acetone was treated with 1 ml of 10% caustic soda. After 1 h, a solution of 1.5 g of sodium acetate in 3 ml of water was added to the resulting solution, the mixture was cooled to 0°C, and, slowly, with stirring, a solution of the arenediazonium salt was added (diazotization was performed with 0.003 mole of an arylamine containing no electropositive substituent, 4 ml of water, 1 ml of concentrated hydrochloric acid, 0.2 g of sodium nitrite in 1 ml of water, and 5 g of ice with a diazotization time of 1 h). After 16 h, the acetone was evaporated off in vacuum. The product was extracted with 25 ml of diethyl ether (or the precipitate was filtered off and dried). The ethereal layer was separated off and evaporated to dryness. The residue was dissolved in 25 ml of benzene and chromatographed on alumina (layer 6 cm high and 1 cm in diameter). The second, yellow, zone was collected. The eluate was evaporated in vacuum to constant weight of the residue, which consisted of one of compounds (VIIa-e). They were yellow-to-brown products melting with decomposition at low temperatures and readily soluble in acetone, ether, benzene, and ethanol, and insoluble in water (Table 2).

2-Arylazothio-5-ethyl-2-thiazolin-4-ones (VIIIa-d). These were obtained in a similar manner to (VIIa-e) from arylamines containing electropositive substituents (see Table 3). They are light-yellow to yellow-brown crystalline products with higher melting points than compounds (VIIa-e) but with physical properties similar to (VIIa-e) except that they melt with deflagration. They react with β-naphthol to form azo dyes. For example, 0.28 g (0.001 mole) of 5-ethyl-2-(p-methoxyphenylazothio)-2-thiazolin-4-one was dissolved in 5 ml of benzene, and 0.1 g (0.001 mole) of β-naphthol was added. The solution was left to stand at room temperature for a week. Then 5 ml of water was added to the mixture and it was chromatographed as described above. The second, dark-red, zone was collected. After evaporation of the solvent to constant weight of the residue, the colorless 1-(p-methoxyphenylazo)-2-naphthol was obtained with mp 132-134°C; according to the literature [12], mp 139-140°C. Yield 33%. Found: N 9.9%. $C_{17}H_{14}N_2O_2$. Calculated: N 10.1%.

TABLE 4. 5-Arylhydrazono-2-arylthio-2-imidazolin-4-ones (XIVa-c)

Compound	Decomp. pt., °C	Empirical formula	Found, %				Calc., %				Yield, %
			C	H	N	S	C	H	N	S	
XIVa	81—82	$C_{15}H_{12}N_4OS$	61,2	4,1	18,7	10,6	60,8	4,1	18,9	10,8	23
XIVb	132—133	$C_{17}H_{14}N_4O_2S$	—	—	17,0	—	—	—	16,6	—	5
XIVc	109	$C_{19}H_{18}N_4O_4S$	57,0	4,6	14,2	8,1	57,3	4,5	14,1	8,0	10

5-Arylhydrazono-2-arylthio-2-imidazolin-4-one (XIVa) and 1-Acetyl-5-arylhydrazono-2-arylthio-2-imidazolin-4-ones (XIVb and c) (see Table 4). These were obtained in a similar manner to (VId). Instead of (IV), the 5-arylhydrazonothiohydantoin (XVa) or the 1-acetyl-5-arylhydrazonothiohydantoin (XVb) was used. If the reaction was performed with compound (XII; R = H), the yield of (XIVa) fell from 23 to 5%.

Alkaline Hydrolysis of (VIb) and (VIIb). A mixture of 0.3 g of the compound concerned, 2 ml of 10% NaOH, and 3 ml of ethanol was heated on the water bath, and then the ethanol was distilled off and the residue was filtered from the solid matter. The filtrate was acidified, and the precipitate that deposited was filtered off immediately. Thiophenol was detected qualitatively [13, 14] in a sample of the filtrate obtained. After a day, the di(p-chlorophenyl) disulfide that had deposited from the filtrate was filtered off and dried. mp 70-72°C; according to the literature [15] 71-72°C. Tests for p-chlorphenol [14] of the mother solution and the steam distillate were negative.

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